South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde
P.O. Box 643, Cape Town Posbus 643, Kaapstad

Cape Town, 7 July 1956 Weekly 2s. 6d. | Vol. 30 No. 27 | Kaapstad, 7 Julie 1956 Weekliks 2s. 6d.

CONTENTS : INHOUD

South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde
P.O. Box 643, Cape Town Posbus 643, Kaapstad

Cape Town, 7 July 1956 Weekly 2s. 6d. | Vol. 30 No. 27 | Kaapstad, 7 Julie 1956 Weekliks 2s. 6d.

DYSPLASIA EPIPHYSEALIS MULTIPLEX

REPORT OF A CASE IN A BANTU CHILD

E. COPE, M.B., B.CH., *Orthopaedic Registrar*

C. MORRIS, CH.M. *Orthopaedic Surgeon*

S. H. GETZ, M.B. CH.B., D.P.H., D.M.R.D., *Radiologist*

Coronation Hospital, Johannesburg, and University of the Witwatersrand

The above name was first introduced by Fairbank[1] in 1935, when he differentiated the condition from dysplasia epiphysealis punctata. However, Jansen[2] in 1934, reported under the name of epiphyseal dysostosis a case which Fairbank considered to be one of dysplasia epiphysealis multiplex. By 1947, 26 cases had been collected by Fairbank. From time to time in various journals other cases have been reported but the total number of cases recorded is extremely small. In the last 10 years no case has been recorded in the *South African Medical Journal* and we believe the following case report to be the first in a Bantu.

The etiology of dysplasia epiphysealis multiplex is entirely unknown. It affects both sexes, males more frequently than females. The age at which the developmental error was recognized in Fairbank's cases varied from 18 months to 14 years, with two exceptions, a girl of 20 years and a middle-aged woman. Hereditary and familial influences are not as a rule in evidence. However, two sisters were described by Gardner Hill (1937), a mother and her twin boys by Resnick[3] (1943), sisters and twins in Fairbank's series; and 3 sisters are reported by Waugh[4] (1952). Jackson *et al.*[5] (1954) trace a family tree of one of their cases which indicates a simple dominant genetic inheritance; however, they are doubtful whether this law holds in general for the condition, since most cases reported have been sporadic.

The radiological features are characterized by:

(*a*) Irregularity in contour and in bony structural pattern of the developing epiphyses.

(*b*) Multicentric epiphyseal ossification.

(*c*) Late appearance, slow development and delayed fusion of the epiphyses.

(*d*) Varying irregularity of adjacent metaphyses.

Epiphyses commonly affected are those of the hips, knees, ankles, shoulders, elbows, the metatarsal and metacarpal bones, the carpal and tarsal bones, and the phalanges of both hands and feet. The vertebrae, skull, teeth and acetabuli are singularly free of abnormality. While the metaphyseal ends of the bones adjacent to the affected epiphyses may also exhibit irregularity, the shafts of the long bones are normal in shape and structure. The lesions are characteristically bilateral, and usually symmetrical.

Information about the histological pathology has been scanty indeed, and Fairbank states that he knows of only one case in which it was investigated, when mucoid degeneration of the cartilage was found irregularly placed among scanty bone-cells.

The blood report is usually normal.

CASE REPORT

Patient M, a Bantu male child aged 10 years, complained of pain over the anterior aspect of his left hip joint. The pain was dull in nature, did not radiate, and was worse on walking and playing. This pain was related to a fall.

The patient is the 8th of 9 siblings. He was a full-term infant and was breast-fed until the age of 2 years. Teething started at the age of 6 months, crawling at 7 months and walking at 10 months. He has not had any childhood illnesses. He was born in the Cape Province, near Queenstown, but has lived in Johannes-

burg since the age of about 4 months. He attends school, and is above average intelligence, being in grade II and always coming first in class, and participates in football.

Family history: the mother, father and all the children are well.

Examination. A bright, intelligent Bantu male child presented, slightly dwarfed but no obvious deformity in spine, limbs or gait was noticed except for some broadening and slight adduction of both fore-feet. The fingers were short and stubby but relatively proportional, and hyper-extension was possible at the proximal inter-phalangeal joints. The ligaments of the other joints of the body were normal.

The patient when first seen in the out-patient department had some limitation of movement at the left hip-joint and both hip-joints were therefore X-rayed. When he was subsequently re-examined in the ward about 1 week later, no limitation of movement was found. The shape of the bones, clinically, was normal, with no widening at the metaphyses or tenderness on palpation.

Measurements. (1) Height of patient 50½ inches. (2) Arm span 53 inches. (3) Upper segment (top of head to pubis) 24½ inches. (4) Lower segment (pubis to ground) 26 inches. (5) Circumference of head 21¾ inches. (6) Left femur 13¼ inches; right femur 14 inches. (7) Left tibia 12½ inches; right tibia 12¾ inches. (8) Left humerus 9¼ inches; right humerus 9 inches. (9) Left radius 8⅛ inches; right radius 8 inches.

Blood Investigation. (1) White blood-cells 8,200 per c.mm. (2) Haemoglobin 14·3 g. (3) ESR 12 mm. in 1 hour. (4) Calcium 5·2 mEq/litre. (5) Phosphorus 4·0 mg./100 c.c. (6) Alkaline phosphatase 31 units. (7) Urea 17 mg./100 c.c. (8) Potassium 5·1 mEq/litre. (9) Sodium 14 mEq/litre. (10) Chlorides (as Na Cl) 540 mg./100 c.c. (11) CO_2 combining power 46 m 1/100 c.c.

Urinary Analyses. (1) Microscopic—nothing abnormal detected. (2) Chemical—nothing abnormal detected. (3) The total volume of urine for 24 hours was 2,570 c.c. and the content of 17-Ketosteroids (estimated as dehydro-iso-androsterone) 4·5 mg.

It should be noted that only the alkaline phosphatase was raised in the above estimations.

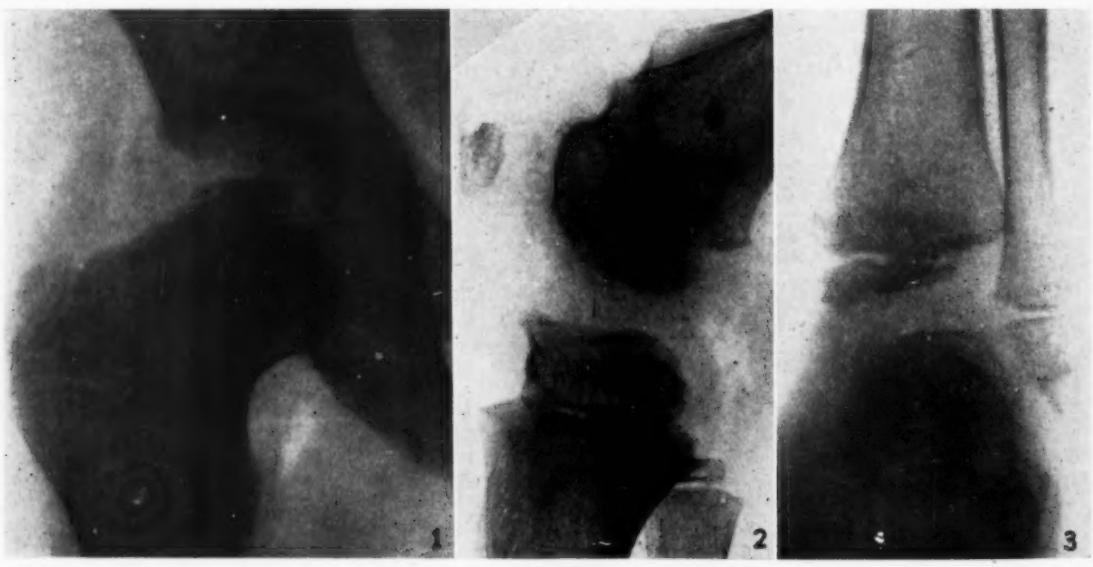
Histological Report. Section of this specimen from the lower epiphysis of the right fibula, shows the presence of atypical hyaline cartilage, in which the cells are irregular and scattered and have little pattern of orientation. Small fragments of osseous tissue are present within the cartilage, but there is little evidence of endochondral ossification. The margins of the cartilage are lined by flattened cells, lying adjacent to loose fibrous connective tissue, containing blood vessels.

Radiological Report

The findings on radiological examintation of the skeleton were as follows:

Hip Joints (*Fig.* 1). The right capital epiphysis shows marked flattening, increased density, fragmentation and several ossific centres. On the left side the capital epiphysis is somewhat larger, slightly flattened, and irregular in outline. Medically a few small ossific centres are shown. The adjacent metaphyseal outline on both sides is irregular and both femoral necks are widened. The epiphyses of the greater trochanters show slight irregularity in outline. The acetabuli are normal.

Knee Joints (Fig. 2). The epiphyses at the lower ends of the femora are large, flattened and markedly irregular, and show some spiky projections. Several small additional centres are present. The tibial epiphyses



Figs. 1, 2 and 3

are triangular in shape and slightly irregular in outline. Lateral views reveal small irregular patellae with spur formation. The fibular epiphyses are not remarkable, but all the epiphyses at the knees show coarse trabecular structure.

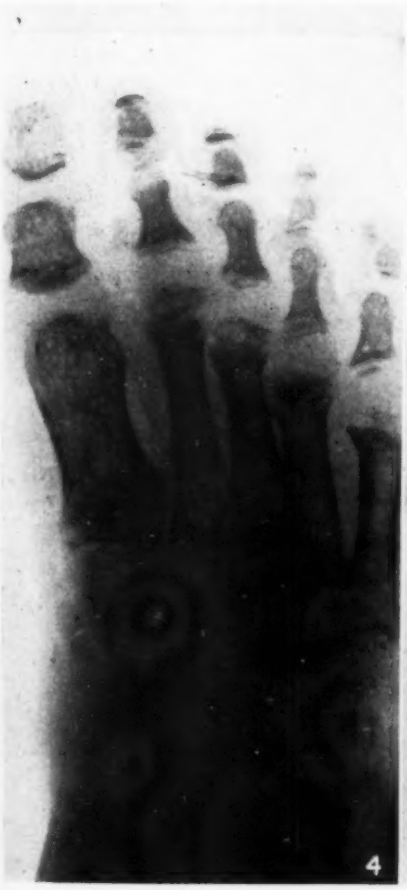
Ankle Joints (Fig. 3). The lower tibial epiphyses are dense and unduly wedge-shaped with marked tapering laterally and producing characteristic obliquity of the articular surface (this triangular appearance is said to occur in 50% of cases studied). The lateral malleoli are low in position. On either side there is a large irregularly-shaped ossific centre, below which several small elongated subsidiary centres are present. There is striking irregularity of the metaphyseal ends of both tibiae.

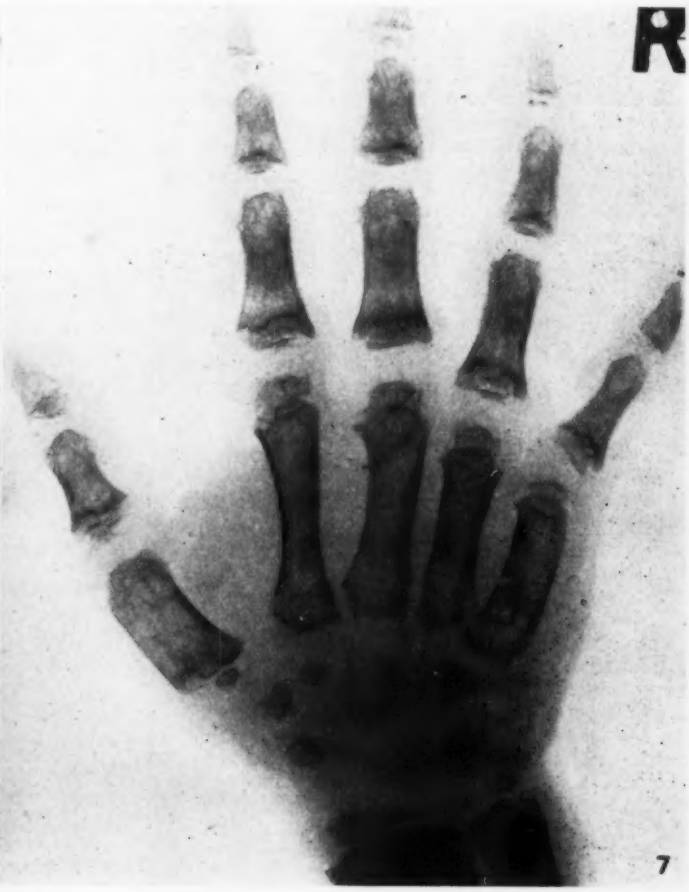
Feet (Fig. 4). All the epiphyses show marked irregularity in contour and in degree of mineralization. In many instances multiple centres are seen. The metatarsals show numerous discrete punctate centres. These bones are short and broadened, with irregular and rather notched ends, and coarse trabeculation can be seen both proximally and distally. The phalanges are broad and stumpy, with coarsely woven pattern throughout, especially in the big toes. The navicular bones show increased density and antero-posterior compression, presenting the appearance of osteochondritis (Kohler's disease). The other tarsal bones also show slight irregularity in form, and coarse trabeculation. The striking feature in both feet is the symmetry in the disposition and character of the lesions.

Shoulder Joints (Fig. 5): These show flattened epiphyses arising from several separate centres.

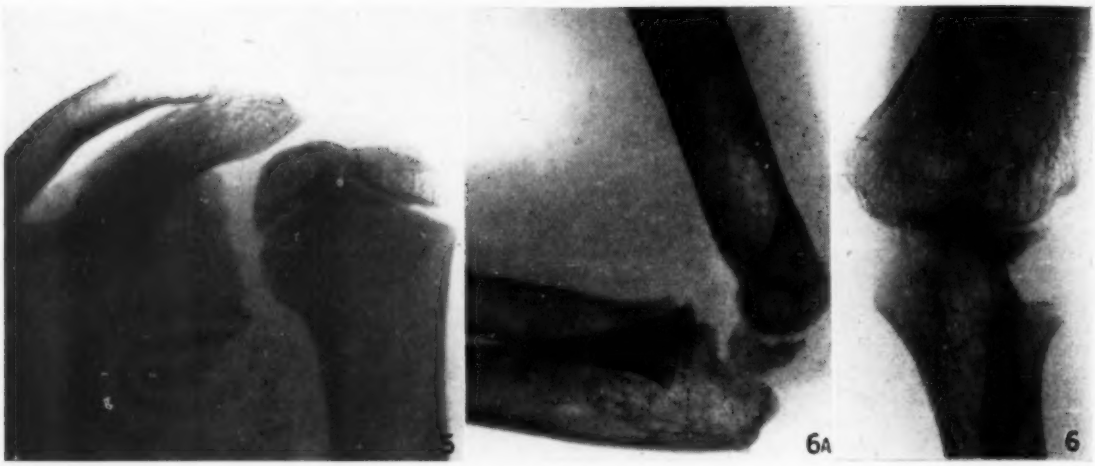
Elbow Joints (Fig. 6). Only the epiphyses of the capitellum, the internal epicondyle and the head of the radius are present. The capitellar epiphyses are dense, and present an irregular stippled appearance.

Hands and Wrists (Fig. 7). Only 6 ossific nuclei are present in the wrists. Bony age is thus retarded. The carpal bones are grossly irregular in form, and this is shown particularly in the capitate and hamate, where sharp spiky projections are present. The distal radial epiphysis is flattened, dense and irregular, and the ulnar centre is very small. Some increased density and





Figs. 4 and 7



Figs. 5, 6 and 6a

irregularity of the adjacent metaphyses is shown. The metacarpals and phalanges are short and broad, with irregular ends and abnormal pattern of cancellous structure. The irregularity of the epiphyses is well demonstrated in the bones of the hand, similar to the changes noted in the feet.

Radiographs of the spine, skull and teeth did not reveal any abnormality.

DIFFERENTIAL DIAGNOSIS

Perthes' Disease. When the signs of bilateral Perthes' disease are found in a patient below the average height it is advisable to radiograph some of the other joints, e.g. shoulder, hips and ankles. Perthes' disease occurs bilaterally in 15% according to Howorth[7] and 7·5% according to Morris.[6] The pathology is different in the two conditions. At any one stage the epiphyses in dysplasia epiphysealis multiplex tend to improve in radiographic appearance, in contrast to osteochondritis, in which the early changes become progressively worse before improvement commences. The abnormal epiphyses in dysplasia epiphysealis multiplex eventually become normal in density, but the outline, though usually smooth, remains permanently irregular. The age at which this permanent definition becomes apparent seems to vary considerably in different cases.

Cretinism is excluded on the general examination. In cretinism the stubby fingers are approximately of equal length. Delay in fusion at the epiphyseal lines in cretins is associated with a band of sclerosis in the terminal layer of the metaphyses.

In *Dysplasia Epiphysealis Punctata* the abnormalities generally are much grosser. The shafts of the long bones are short and thick. Many of these patients die before the age of 1 year and half the cases have congenital cataracts.

In *Morquio-Brailsford Disease* (*Osteochondrodystrophy*) the acetabuli appear markedly enlarged and irregular on X-ray. The spine exhibits special features, viz. the shape of the bodies and in many cases kyphosis. The central prolongation of the bodies with the forward-projecting tongue is quite distinctive and diagnostic.

In *Dyschondroplasia* (*Ollier's Disease*) the epiphyseal changes are comparatively insignificant and are entirely overshadowed by the changes in the metaphyses, which contain unossified cartilage. The changes tend to be unilateral.

In *Osteopoikilosis* the epiphyses are of normal shape. The discrete dense spots characteristic of this condition are not confined to the epiphyses.

In *Osteopetrosis* some epiphyses occasionally show irregularity in density but changes in the shafts dominate the picture.

Pituitary Gigantism. Mottled epiphyses have been described in association with pituitary gigantism.

SUMMARY

A case of dysplasia epiphysealis multiplex is described, believed to be the first case reported in a Bantu. The clinical and radiographic appearances are typical. The results of blood and urinary investigations are recorded and the histological pathology of the case described. The differential diagnosis of this condition is discussed.

We should like to thank Dr. Dorfman, of the South African Institute of Medical Research, for his interest in the case and for the histo-pathological description. For permission to publish the case, we are grateful to the Superintendent of the Coronation Hospital.

REFERENCES

1. Fairbank, T. (1951): *An Atlas of General Affections of the Skeleton*, p. 91. Edinburgh: Livingstone.
2. Jansen, M. (1934): Z. Orthop. Chir., **61**, 253.
3. Resnick, E. (1943): J. Bone Jt. Surg., **25**, 461.
4. Waugh, W. (1952): *Ibid.*, **34B**, 82.
5. Jackson, W. P. U., Hanelin, J. and Albright, F. (1954): Arch. Intern. Med., **94**, 886.
6. Morris, C. (1952): *Perthes' disease—A clinico-pathological study.* Thesis, Univ. Witwatersrand.
7. Howorth, M. B. (1953): *Textbook of Orthopedics*, 3rd ed., p. 673. Philadelphia: Saunders.

South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde

REDAKSIE

PYN IN DIE BORS

Die vraagstuk van borspyn is onlangs bespreek by 'n samespreking wat aan die Mayo Clinic[1] gehou is. Die ingewikkeldheid van hierdie onderwerp is duidelik uit die groot aantal oorsake wat aanleiding kan gee tot pyn in die bors—die pyn kan ontstaan uit die senuwees, spierskelet, hartbloedvate, slukderm, middelvlies, borsvlies, longe, middelrif, en uit die organe van die buik. 'n Paar punte uit die 5 referate wat by die samespreking gelewer is sal hier bespreek word; die oorspronklike artikels behoort egter in geheel gelees te word.

Beserings binne-in die rugmurg veroorsaak nie gewoonlik pyn nie; wanneer die pyn wel voorkom, is dit meer waarskynlik die gevolg van druk op die agterwortelvesels as van irritering van die rugmurgbane. Irritering van die agterwortels is 'n algemene oorsaak van pyn in die bors en kan aan verskeie kondisies gewyt word, wat dan ook oorweeg moet word: ribbebreuk, samepersing deur 'n gewas, 'n uitgesakte skyf, 'n sweer, ontstekingsletsels, bloedvatletsels (slagaarverharding, ontsteking van 'n slagaar-buitewand, tussenwand-slagaarbreuk) en stoornisse in die stofwisseling (suikersiekte, porfiria).

Die algemeenste oorsaak van pyn in die borswand is moontlik spiervermoeidheid en ooreising—miskien die gevolg van ongewone oefening, swak liggaamshouding, of beroep. Dit word dikwels oor die hoof gesien dat pyn in die agterste gedeelte van die borskas veroorsaak kan word deur ontsteking van die epifises van die werwels, wat deur ontaarding gevolg word; dit moet by ouer pasiënte vermoed word. Miëloom is waarskynlik die algemeenste gewas van die borswerwels en moet in gedagte gehou word by pasiënte wat die ouderdom van 45 jaar bereik het. Ettervormende beenontsteking van die werwels is 'n siektetoestand wat vandag meer dikwels uitgeken word.

T. J. Dry bespreek borspyn wat uit die hartbloedvaatstelsel spruit. Die pyn kan te wyte wees aan *plaaslike bloedloosheid van die hartspier* weens kroonslagaarsiekte, hoewel letsels van die aorta ook die oorsaak kan wees. Akute hartspierverstopping kan die eerste teken van kroonslagaarsiekte wees met die beklemmingspyn uitgestraal na die maagkrop (‚akute slegte spysvertering'). Ook kan kwaai aanvalle voorkom wat paar uur duur en wat gepaard gaan met die verskynsels van ernstige skok; by ander gevalle is daar kwaai dispnee sonder enige pyn (miskien net 'n ligte brandende gewaarwording), met of sonder tekens van akute linker-

EDITORIAL

THORACIC PAIN

In a symposium recently held at the Mayo Clinic[1] the question of thoracic pain was discussed. The complexity of the subject is revealed by the numerous causes of pain in the thoracic region, from neural, musculo-skeletal, cardiovascular, oesophageal, mediastinal, pleural, pulmonary, diaphragmatic, and abdominal structures. A few points from the 5 papers presented at the symposium are considered here; the original articles should be read in full.

Intramedullary lesions of the spinal cord do not usually produce pain; when pain does occur it is more likely to be the result of pressure on dorsal root fibres than of irritation of intramedullary tracts. Irritation of the dorsal roots is a common cause of thoracic pain and may be due to a variety of conditions, which have to be considered: rib fracture, compression by tumour, prolapsed disc, abscess, inflammatory lesions, vascular lesions (arteriosclerosis, periarteritis, dissecting aneurysm) and metabolic disturbances (diabetes, porphyria).

The commonest cause of pain arising in the chest wall is possibly muscle fatigue and strain, the result perhaps of unaccustomed exercise, poor posture, or occupation. In the posterior part of the chest epiphysitis of the vertebral bodies followed by degenerative changes is frequently overlooked as a cause of pain; it should be suspected in elderly patients. Myeloma is probably the commonest tumour of the thoracic vertebrae and should be suspected in patients who have reached the age of 45 years. Pyogenic osteitis of the vertebrae is a condition that is coming to be recognized more frequently.

Thoracic pain of cardiovascular origin is discussed by T. J. Dry. The pain may be due to *myocardial ischaemia* from disease of the coronary arteries, although aortic lesions may also be the cause. Acute myocardial infarction may be the first indication of coronary disease, with anginal pain referred to the epigastrium ('acute indigestion'), or severe seizures may occur lasting many hours and associated with features of severe shock; in other cases there is severe dyspnoea,

kamerversaking. Ook kan borspyn deur *irritering van die hartsak* veroorsaak word, maar ontsteking van die hartsak kan ook sonder pyn voorkom. Wanneer pyn wel voorkom, kan dit tot 'n bepaalde streek beperk wees (onder die borsbeen, om die hart, op die krop van die maag, of onder die blaaie), of dit kan tot die nek en selfs die arms uitstraal. In teenstelling met die elektrokardiografiese beelde van hartspierverstopping, is daar nooit 'n daling van die RS-T segment nie, en daar is ander belangrike onderskeidende verskynsels. Sekere siektes van die *aortaboog-stelsel* veroorsaak pyn, en verskeie meganismes kan daarby betrokke wees. 'n Tussenwand-slagaarbreuk van die aorta kan dus pyn veroorsaak wat nie onderskei kan word van die pyn van hartspierverstopping nie, en dit moet vermoed word as herhaalde elektrokardiogramme bv. onveranderd bly. Hoofslagaarbreuk word vandag maar selde gesien omdat sifilis so doeltreffend op vroeë stadium behandel word.

Verskeie toestande kan slukdermpyn veroorsaak. Dit mag angina pectoris naboots maar staan nie altyd in verband met slukmoeilikheid nie. Hoewel hierdie pyn gewoonlik onder die borsbeen setel, kan dit na die nek en gesig, die skouers, die arms, of die rug versprei. Die pyn van 'n hiatus-breuk kan kroonslagaargebrek naboots. Gewasse van die slukderm of van die middelvlies veroorsaak nie gewoonlik pyn nie tensy ander organe daarby betrokke raak.

Die long en sy oortreksel, die longborsvlies, is ongevoelig vir pyn. Daar is dus sekere soorte longletsels wat nie noodwendig met pyn gepaard gaan nie. Pyn weens longletsels word veroorsaak as naburige organe in die gedrang kom—borswand, middelrif, die lugpyp en sy vertakkings—of deur bloedvaatkramp, of verplasing van die ingewande.

Pyn weens verspreide vaatkramp word hoofsaaklik veroorsaak deur propvorming of drukverhoging in die longbloedvate. Sommige mense meen dat die vrystelling van 5-hidroksitriptamien 'n rol speel by die eerste kondisie.[2] Die pyn van drukverhoging in die longslagare kan baie op angina pectoris lyk, maar kan gewoonlik nie met gliseriel trinitraat verlig word nie.

Wat die buikaandoenings betref, het galsteenkoliek, akute alvleesklierontsteking, en perforasie van die buik-organe reeds pyn in die bors veroorsaak wat verkeerdelik aan akute hartspierverstopping toegeskryf is. Die pyn van die bo- en onderkant van die middelrif kan nie onderskei word nie, maar dit is wel moontlik om te onderskei tussen ontsteking van die borsholtevlies oor die middelrif, en inflammasie van die buik-organe.

Baie van die siektes wat pyn in die borsstreek kan veroorsaak is al verkeerdelik aangesien vir akute hartspierverstopping. Dit is belangrik om te besef dat pyn uit die spierskeletstelsel na die arms kan uitstraal, want hierdie simptoom kan aanleiding gee tot 'n verkeerde diagnose van hartsiekte. 'n Noukeurige geskiedenis en ondersoek behoort die juiste oorsaak van die pyn te ontmasker; wanneer die simptome en die bevindings nie ooreenslaan nie, raai Dry aan dat die nadruk liewer op die simptome as op die bevindings gelê moet word.

1. Samespreking (1956): Proc. Mayo Clin., **31**, 1.
2. Van die Redaksie (1956): Lancet, **1**, 240.

with complete absence of pain (perhaps a mild burning sensation), with or without signs of acute left ventricular failure. Thoracic pain may also be due to *pericardial irritation*, but pericarditis can occur without pain. When pain occurs it may be localized (substernal, pericardial, epigastric, or in the scapular region), or it may extend into the neck and even to the arms. In contrast with the electrocardiographic features of myocardial infarction there is no depression of the RS-T segment at any time and there are other important differentiating features. Certain diseases of the *aortic arch system* cause pain and several mechanisms may be involved. Thus dissecting aneurysm of the aorta can produce pain indistinguishable from that due to myocardial infarction and is suspected if, for instance, repeated electrocardiograms remain unchanged. Aneurysm of the aorta is rarely discovered nowadays because syphilis is effectively treated in its early stages.

Oesophageal pain may be due to a variety of conditions. It may simulate angina pectoris and is not always associated with dysphagia. While usually substernal, it may extend to the neck and face, the shoulders, the arms, or the back. The pain of hiatal hernia may simulate coronary insufficiency. Tumours of the oesophagus or of the mediastinum do not usually cause pain unless they involve other structures.

The lung and its covering of visceral pleura are devoid of pain sensation. There are therefore certain types of pulmonary lesion that may not be associated with pain. The pain from pulmonary lesions is due to involvement of adjacent structures—chest wall, diaphragm, trachea or bronchi—to vascular spasm, or to displacement of the viscera.

Pain due to diffuse vascular spasm is produced mainly by pulmonary embolism and pulmonary hypertension. In the former condition the release of 5-hydroxytryptamine has been considered to play a role.[2] The pain of pulmonary hypertension may resemble angina pectoris closely but is generally not relieved by glyceryl trinitrate.

Abdominal conditions such as biliary colic, acute pancreatitis and perforation of the abdominal viscera have caused pain in the chest which has been attributed to acute myocardial infarction. There is no distinction between pain from the upper and lower surfaces of the diaphragm, but it is possible to differentiate diaphragmatic pleurisy from inflammation of the abdominal viscera.

Many of the conditions that may produce pain in the thoracic region have been mistaken for acute myocardial infarction. It is important to recognize that pain from musculo-skeletal structures may extend to the arms, for this symptom may lead to a wrong diagnosis of cardiac disease. A careful history and examination should reveal the true cause of the pain pattern; when the symptoms and findings are incompatible the emphasis, according to Dry, should be placed on the symptoms rather than on the findings.

1. Symposium (1956): Proc. Mayo Clin., **31**, 1.
2. Editorial (1956): Lancet, **1**, 240.

STRAINS OF SINDBIS-LIKE VIRUS ISOLATED FROM CULICINE MOSQUITOES IN THE UNION OF SOUTH AFRICA

I. ISOLATION AND PROPERTIES*

M. P. WEINBREN, B.Sc. HONS. (RAND), M.R.C.S., L.R.C.P.†

Staff Member, Poliomyelitis Research Foundation, South African Institute for Medical Research

R. H. KOKERNOT, M.D., D.V.M., M.P.H.

and

K. C. SMITHBURN, B.Sc., M.D.

Staff Members, Rockefeller Foundation

During the latter part of 1953 a unit was established in Johannesburg to investigate arthropod-borne virus diseases. This unit is supported financially by the Poliomyelitis Research Foundation, the South African Institute for Medical Research, and the Rockefeller Foundation. It functions with the support and collaboration of the Union Health Department and Division of Veterinary Services of the Department of Agriculture. The programme included immunity surveys to determine what viruses occur and how prevalent they are, the collection of blood samples from patients with febrile illness for attempted isolation of virus, and the collection of haematophagous arthropods for attempted virus isolation. The arthropod collections were undertaken by the Medical Ecology team under the direction of Mr. David Davis, Government Ecologist, with the advice and collaboration of Dr. Botha de Meillon of the South African Institute for Medical Research. Suitable working sites within reasonable distance of Johannesburg were selected and it was from mosquitoes caught at one of these that we were able to isolate our first strain of virus. The site was in Springs, a town situated 30 miles eastward from Johannesburg.

In Springs the mosquito-catching team was based on a house overlooking a portion of open veld in which there was a small pan, about which the greater part of the catching was done. The distance between the house and the pan is about 400 yards and the prevailing wind across the pan blows from the direction of the house. The mosquitoes from which the virus designated AR 86 was isolated were captured in the house.

The other two strains of virus to be discussed in this paper were isolated from mosquitoes taken at Isis Estates, situated at Babsfontein, 33 miles NNE of Johannesburg. This is a well-ordered farm on which Messrs. I. and A. L. Bader maintain a large herd of pedigree Friesland cattle. Resident on the farm with their respective families are a veterinarian who is the farm manager, an agricultural officer and an assistant manager. The Native population on the farm may be divided into two groups, one of relatively-static permanent residents numbering about 140, and the other an extremely variable population of about 30 casual labourers.

Attention was first drawn to Isis Estates when the veterinary authorities at Onderstepoort notified us of an outbreak of illness in cattle there. When inquiry was initiated it was learned that there had also been a number of cases of febrile illness in human beings. In the course of our attempts to discover the aetiology of these outbreaks the virus strains designated AR 166 and AR 169 were isolated.

MATERIALS AND METHODS

The mosquitoes caught at Springs from which the first strain of virus was isolated were taken while at rest in the house, while the mosquitoes from Isis Estates which yielded the other two strains of virus were caught by hand with human bait, by sweeping the grass with nets, and in Magoon traps baited with calves. They were identified while living and then were placed in a −20°C cold room until ready for processing. Generally speaking, a 'lot' of arthropods consisted of all the individuals of a given species caught in a certain locality in one catch or series of catches. Whenever pooling of species was resorted to, a 'lot' contained more than one species but only arthropods caught at the same place in a given catching period. Each 'lot' was given a serial number in the 'AR' series, and virus strains derived therefrom carried the 'name' of the arthropod 'lot', such as virus AR 86. The mosquito lots were triturated and suspended in 10% heat-inactivated normal rabbit serum in 0·85% solution of sodium chloride.* The amount of diluent used was at the rate of 1 ml. of fluid to each 10 mosquitoes. This rule was adhered to until the rate of 100 mosquitoes to 10 ml. was reached, above which this quantity of fluid was deemed sufficient for any number of mosquitoes up to 500. Penicillin (500 units/ml.) and streptomycin (0·0005 g./ml.) were then added and well mixed. The resultant suspension was centrifuged at room temperature at 2,500 r.p.m. for 20 minutes in an angle head. The supernatant fluid was drawn off and transferred to sterile tubes, which were then allowed to stand in the 4°C refrigerator until an hour had elapsed from the time of antibiotic addition. Inoculations were then made into both newborn and adult mice.†

The inoculations were made into infant mice between the ages of 24 and 48 hours according to a method similar to that suggested

* The investigations upon which this report is based were financed jointly by the Rockefeller Foundation, the Poliomyelitis Research Foundation (South Africa), and the South African Institute for Medical Research, and were conducted under the sponsorship and with the collaboration of the Union Health Department and the Veterinary Division of the Department of Agriculture.

† Present address: Virus Research Institute, P.O. Box 49, Entebbe, Uganda.

* At the time at which these isolations were made, 'bovine plasma albumin' (Armour's fraction V) was not available, but shortly thereafter supplies arrived, and a 0·75% concentration suspended in a phosphate buffer of pH 7·6 was used whenever infected material was suspended for passage.

† The newborn mice were supplied from the colony run for the Poliomyelitis Research Foundation by Mr. C. Brandt, and the adults from the colony maintained for the Serum Laboratories of the South African Institute for Medical Research by Dr. J. H. Mason. The latter were young animals of either sex weighing approximately 16 g.

by Dr. R. M. Taylor[1]. A 0·25 ml. 'tuberculin' type syringe is used, fitted with a short 27-gauge needle, and the needle is inserted under the skin between the scapulae and then run cephalad until it enters the right side of the cranium, where 0·01 ml. is deposited. The needle is then partly withdrawn and a second dose of 0·01 ml. is deposited over the fat pad. The adult mice were anaesthetized with ether and received a 0·03 ml. inoculum into the left cerebral hemisphere. Inoculated mice were observed for 21 days.

Whenever mice sickened from causes that were not obviously non-specific, some were sacrificed, a portion of the brain or carcasses so obtained being sealed in a glass tube and stored as frozen reference material. The remainder of the material from the sacrificed mice was passed to groups of infant and adult mice as a 10% suspension. Blood-agar slopes and nutrient broth were inoculated to exclude infection by the commoner bacterial pathogens as the cause of illness. When the material for bacteriological study had been taken, penicillin and streptomycin were added to the suspension, which was then centrifuged and, after an hour of antibiotic contact, was inoculated, the residue being stored at −20°c.

It was discovered that the layer of fatty material which is sometimes found on the surface of the carcass supernate should be carefully avoided because it contains substances which are extremely toxic for mice on intracerebral inoculation.

Whenever a second passage series of mice sickened a further passage was made, again controlled by bacterial cultures in broth and on blood-agar. The passage was, however, carried out in duplicate, once with unfiltered material, and once with suspension which had been passed through a 'Ford's Sterimat grade SB' (an asbestos filter which has approximately the same pore size as a Seitz EK filter) under a pressure of 2 atmospheres of pure nitrogen after washing with 10% normal rabbit serum in saline. Whenever it became apparent that we were dealing with a filter-passing agent, affected mice were sacrificed and used to prepare stock virus, which was put up either in distilled water or saline, a portion of each suspension being frozen and the remainder lyophilized. In either case the stock was stored in the CO_2 box.

It was found that the frozen preparations put up in water deteriorated rapidly, though the desiccated preparations were more stable. Later, when stocks of known non-immune monkey sera became available this was used as menstruum and gave very stable stocks of virus when used for making either frozen or lyophilized preparations.

Specific immune sera for each strain of virus were produced by immunization of *Cercopithecus aethiops pygerythrus* F. Cuvier monkeys. These animals proved quite satisfactory for this purpose when inoculated intracerebrally or subcutaneously with a suspension of virus-infected mouse brain.

In the early passages, tissues were taken from sacrificed mice, fixed in Bouin's fluid, sectioned, and stained with haematoxylin and eosin for histological studies. In all the experiments the degree of virus activity was assessed by means of the 50% end-point calculated by the method of Reed and Muench[2].

Protection tests were carried out on paired litters of randomized infant mice.* Each infant mouse received an intracerebral inoculation of 0·02 ml. of a mixture containing equal parts of serum and virus suspension which had been incubated in a water bath at 37°C for 1 hour. The virus suspension was of such a dilution that each inoculum contained approximately 100 LD_{50}. Each neutralization test was controlled by a titration in known non-immune serum to assess the dose of virus used, and a titration in known immune serum as a specificity check.

ISOLATION

On 12 February 1954 mosquito lot AR 86, caught at Springs on 10 February, was processed. This lot was made up by pooling 4 *Culex* (*Culex*) *pipiens* Linnaeus* or *Culex* (*Culex*) *fatigans* Wiedemann,* 13 *Culex* (*Culex*) *univittatus* Theobald, and 2 *Culex* (*Culex*) *theileri* Theobald.

On 15 February 5 of the 7 inoculated infant mice were dead and the remaining 2 were sick, though the adult mice remained well throughout the period of observation. A passage of carcasses to a litter of infants and a group of adult mice was made.

On 19 February 3 of the 7 infants inoculated on 15 February were dead and the surviving 4 were sick. The latter were all sacrificed for histological study, for storage of carcass stock in the frozen state, and for a passage of brain emulsion and passage of carcass suspension. On the same day the original arthropod suspension was thawed and inoculated into a litter of infant mice and a group of adult mice. This attempt at re-isolation proved successful.

On 22 February all the adult mice inoculated with the various materials derived from mosquito pool AR 86 were quite well, though of the infant mice inoculated on 19 February, many were dead and the remainder sick. The sick infants were sacrificed, and the following experiments were carried out, of which the results are summarized in Table I:

TABLE I. RESULTS OF PRELIMINARY TESTS TO STUDY THE PATHOGENICITY OF STRAIN AR 86 FOR MICE

Inoculum, source	*Route of inoculation*	*Age of mice (days)*	*No. of litters or adult groups*	*Titre or result*
Brain (filtered) ..	IC	1	6	6·5
Brain (unfiltered ..	IC	1	8	7·25
	SC	1	1*	All died
	IP	1	1	All died
	IC	7	1	All died
	IC	10	1	All died
	IC	14	1	2/6 died
	IC	Adult	1	*None died*
Carcass (unfiltered)	IC	1	7	7·4

(IC=intracerebral. SC=subcutaneous. IP=intraperitoneal.

* In those cases where only one litter was inoculated, the mice received a 10^{-1} dilution of virus suspension.)

1. Filtration of brain suspension through a Ford's Sterimat grade SB filter pad. Mice receiving the filtrate sickened and died, attesting to the filterability of the agent.

2. Titrations in infant mice. The unfiltered material titred $10^{-7.25}$ and the filtered material $10^{-6.5}$. (See Table I.)

3. The unfiltered 10% suspension was used to inoculate one litter of newborn mice subcutaneously, one litter of newborn mice intraperitoneally, and single litters of 7-day, 10-day and 14-day old mice, and a group of 6 adult mice, all intra-cerebrally. There was 100% mortality in all the groups aged 10 days or less. Two of the 14-day old mice died, but all the adult mice remained well. (See Table I.)

4. From the litter which received the carcass inoculum on 19 February, one infant mouse was taken for histological study. A titration of carcass suspension gave an incomplete end-point at $10^{-7.42}$. (See Table I.)

5. From the litters which had been inoculated with

* It was found that false results consequent upon non-specific deaths and cannibalism could be greatly reduced by the use of double litters of mice. The results were further improved by randomizing the infants and reducing the number in each litter to 6. The randomizing was effected by removing all the infants from the mothers immediately before the beginning of the inoculations and pooling them in a cotton-wool-lined container. At the time of inoculation, 6 infants were taken at random, inoculated, and placed with the foster mother in the appropriately labelled box.

* As it is not readily possible in this area to differentiate the adult females of these species, they are grouped together.

the thawed original arthropod suspension, 6 carcasses were used for preparation of first-passage stock virus.

The details of the isolation of strains AR 166 and AR 169 from mosquitoes captured at Isis Estates need not be given, because they are essentially similar to those described for strain AR 86. Table II shows the number

TABLE II. MOSQUITO SPECIES INCLUDED IN THE POOLS WHICH YIELDED VIRUS AND THE DATA CONCERNING THE RE-ISOLATION FROM EACH POOL (1954)

Virus strain	*Mosquito species*	*No. of mosq.*	*Place caught*	*Date caught*	*Date to lab.*	*Date inoculated*	*Date of re-isolation*
AR 86	*C. pipiens/fatigans*	4	Springs	10 Feb.	11 Feb.	12 Feb.	19 Feb.
	C. theileri	2					
	C. univittatus	13					
AR 166	*C. univittatus*	12	Isis Estates	13-17 Mar.	15-19 Mar.	19 Mar.	23 Mar.
AR 169	*C. tigripes*	2	Isis Estates	13-16 Mar.	15-17 Mar.	19 Mar.	23 Mar.
	C. annulioris	1		13 Mar.	15 Mar.		

and species of mosquitoes which made up the lots from which the 3 strains were isolated, the time intervals involved in handling them, and the date on which re-isolation of the agent was effected.

HISTOPATHOLOGY

Tissues taken from baby mice infected with these 3 strains showed significant and similar changes in brain and striated muscle. No abnormalities could be demonstrated in smooth muscle, cardiac muscle, fat pad, liver, pancreas, spleen, kidney, thymus or lung. In the brain there was moderate hyperaemia of small capillaries throughout the substance but there was no oedema and no perivascular round-cell infiltration. Many cells in Ammon's horn appeared swollen and showed margination of chromatin, while others were disintegrating. There was also a proliferation of spindle-shaped cells in the supporting structure in this area. Elsewhere in the brain occasional cells showed vesicular degeneration. In some sections diffuse necrosis of ganglion cells could be seen.

In skeletal muscles there was diffuse necrotic change, with foci showing loss of striation and separation and fragmentation of myofibrils, with nuclear pyknosis and karyorrhexis. Some areas were seen in which there was hyaline change and infiltration by lymphocytes. The impression gained from examination of these slides was one of acute encephalitis of viral origin accompanied by myositis.

The changes found in the skeletal muscle were not unlike those produced by some strains of Coxsackie virus, but the encephalitis is not of the pattern one would expect to find in Coxsackie infection. The South African isolates do not cause oedema, perivascular infiltration by lymphocytes, areas of necrosis leading to an appearance of rarefaction, or leptomeningitis, all of which are described by Melnick and Godman.[3] A further differentiating point lies in the fact that one would not commonly find encephalitis and extensive myositis in one animal as the result of a Coxsackie infection. The Coxsackie viruses which attack the brain primarily also cause focal myocardial necrosis, fat necrosis, and sometimes hepatitis and pancreatitis,[3,4] none of which occurs with the South African isolates.

PROPERTIES OF STRAINS AR 86, AR 166 AND AR 169

Pathogenicity and Antibodies. These filter-passing agents are, as isolated, pathogenic for infant mice, though not for adults, the pathogenicity of the agent decreasing with the increase in the age of the mice. An experiment was carried out with strain AR 86 in which comparable titrations were simultaneously set up in infant mice 1, 2, 3, and 4 days of age. The titres obtained from these experiments showed no significant difference, but when the average survival time was calculated for the combined groups receiving dilutions 10^{-2} to 10^{-5} it was seen to exhibit a small but progressive increase. The 1-day-old mice gave an average survival time of 2·0 days, the 2-day-old mice 2·15 days, the 3-day-old mice 2·24 days and the 4-day-old mice 2·69 days. These figures may not be statistically significant, as the groups were small, but they do confirm the impression gained early in the work on these strains that there is a decrease in susceptibility of infant mice as their age increases.

The strains are pathogenic for infant mice by various routes of inoculation. By the intracerebral route they cause death in dilutions as great as 10^{-7}. Most deaths occur within 48 to 72 hours and, when they do, the mice exhibit only tremors and incoordination. However, with very small doses of virus death may be delayed and in these cases may be preceded by paralysis. When paralysis occurs it may affect any of the four limbs. It is not unusual, for instance, to see an infant mouse with unilateral 'wrist drop'.

In order to investigate the pathogenicity of these agents for the grey monkey *Cercopithecus aethiops pygerythrus*, and also in the hope of producing specific immune serum, 2 monkeys were inoculated subcutaneously with 2·0 ml. of 10^{-2} dilution of brains of mice inoculated with strains AR 86 or AR 169. Daily rectal temperatures were recorded but showed no significant change, nor was there any sign of illness. After an interval of 2 weeks the monkeys were bled. That which had been inoculated with AR 169 was found to have developed antibody in sufficient quantity to neutralize more than 5 logs of the homologous virus and also strains of AR 86 and AR 166. The monkey inoculated with AR 86 had only produced sufficient antibody to neutralize about 1 log of virus as compared with a titration in serum from a pre-inoculation bleeding of the same monkey. Two more monkeys were then inoculated intracerebrally, one with strain AR 86 and one with strain AR 166. These received a dose of 0·5 ml. of a 10^{-1} suspension of brain taken from mice inoculated with the respective viruses. After an interval of 2 weeks both these monkeys were found to have developed potent antibodies capable of neutralizing more than 5 logs of all 3 strains of virus. There were no signs of illness in the monkeys even after intracerebral inoculation.

Antibody production without signs of illness also occurs after the intraperitoneal inoculation of unadapted

viruses into adult mice and irregularly after the intraperitoneal inoculation of rabbits and guinea-pigs.*

It has been established that strain AR 169 is lethal for 8-day old chick embryos when inoculated *via* the yolk sac and for day-old chicks when inoculated subcutaneously.

The thermal death points of strains AR 86 and AR 169 have been determined. The method used was as follows:

Four water baths were set up, each consisting of a Pyrex glass beaker of 1 litre capacity containing 600 ml. of water. The temperature of each was kept at the desired level with the aid of a Bunsen burner and a dial-reading thermometer. Each water bath was in the care of a separate technician whose duty was to stir the water in the bath constantly and to take and record the temperature of the bath every minute throughout the course of the experiment. Potent lyophilized samples of the 2 viruses were rehydrated in distilled water to original volume and then diluted with 0·75% bovalbumin to give 10^{-2} suspensions. These were then divided into 5 parts, each being sealed into a pyrex glass ampoule. One ampoule was placed in the 4°C refrigerator to act as control, while others were weighed with lengths of solder and immersed in the water baths. At the end of the period of heating the ampoules were transferred from the water baths to a bath of ice water. Then decimal dilutions were made in 0·75% bovalbumin for inoculation into infant mice. A range-finding experiment was 5arried out with 30 minutes' exposure to temperatures of 45°, c0°, 55° and 60°C, in which virus activity was sought in the heated samples by means of inoculation of infant mice with dilutions of 10^{-2} and 10^{-3}. The results of this experiment indicated that the virus was inactivated by a temperature in the neighbourhood of 55°C. A second experiment was carried out with 30 minutes' exposure to temperatures of 50°, 53°, 56° and 60°C, after which the 10^{-2} suspension which had been heated, and also that which had been kept at 4°C as a control, were titrated in duplicate litters of baby mice. Inspection of the temperature data recorded each minute for each of the water baths, revealed that at no time during the 30 minutes was there a variation of more than 0·5°C in any of the 4 water baths.

The results of this experiment, given in Table III, show that both strains are almost completely inactivated by 30 minutes exposure to a temperature of 56°C, while being relatively unaffected by 53°C. The titres shown for temperatures of 56°C, and higher, are approximations, as the most infective dilution used was 10^{-2}. It may be noted that, though the differences are not large enough to be statistically significant, there is a suggestion that the AR 169 strain is somewhat more sensitive to heat than is the AR 86. This was also noted in the range-finding experiment, where there was a longer average survival-time for the mice inoculated with AR 169 material heated at 55°C than for those inoculated with the equivalent AR 86 material.

TABLE III. STUDIES ON THE INACTIVATION OF VIRUS BY HEAT

Virus strain	*Temperature °C*	*Titre, logs*	*Decrease, logs*
AR 86	4	7·06	—
AR 169		7·27	—
AR 86	50	6·16	0·91
AR 169		6·25	1·02
AR 86	53	5·75	1·31
AR 169		5·38	1·89
AR 86	56	@1·88	@5·18
AR 169		@1·55	@5·72
AR 86	60	@1·54	@5·52
AR 169		no deaths 10^{-2}	

@ Approximate values as the most infective dilution used was 10^{-2}.

An experiment was run to determine *the sensitivity of the AR 86 strain to ether as follows:*

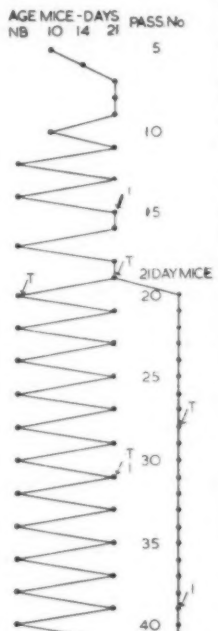


Fig. 1. To show the passages involved in the adaption of the virus to adult mice.

Two ampoules of first-passage lyophilized virus were re-hydrated to original volume with distilled water. This was then further diluted with bovalbumin to give a final concentration of 10^{-2}. This 10^{-2} suspension was then divided into 2 parts. One, the control, was placed in a sterile corked Wassermann tube and the other was mixed with ether in the proportion of 1 part of ether to 4 parts of virus suspension before being placed in a sterile corked Wassermann tube. Both tubes were then placed in the 4°C refrigerator for 24 hours. At the end of this period they were removed, the control was left at room temperature and the test mixture was centrifuged in an angle-head at 3,000 r.p.m. for 20 minutes at room temperature. The virus suspension was then carefully removed from beneath the supernatant ether layer by means of a syringe fitted with a 1·5" 27-gauge needle. To remove dissolved ether, the suspension was subjected to a negative pressure of 22·5 inches of mercury (barometric pressure = 25 inches) for 15 minutes. Decimal dilutions of both virus suspensions were titrated in infant mice.

The control suspension gave a titre of 5·6. The suspension which had been in contact with ether gave a titre of 2·5, showing the virus to be sensitive to ether.

Long-term experiments were done to attempt the *adaptation of AR 86 virus to weaned mice.* A third-passage carcass was used to inoculate newborn mice and a litter of mice approximately 10 days old. Subsequently two passage lines were established as shown in Fig. 1. Specificity tests were done at frequent intervals to assure that the agent in passage was immunologically similar to the original. Adaptive changes were striking and progressive. Titrations from the 2 separate lines at 44th- and 55th-passage levels are shown in Table IV. The titres obtained were respectively $10^{-6.35}$ for the brains of infant mice receiving virus of 44th passage in 21-day mice, $10^{-3.82}$ for the brains of 21-day mice of 44th passage, and $10^{-6.0}$ for the infant-mouse brain of the staggered series at 55th passage. What is possibly of

* A sample of virus AR 86 was supplied to the authorities at Onderstepoort, where certain experiments were carried out under the direction of Dr. R. A. Alexander. One of the experiments involved the inoculation of horses. Some of the immune serum so produced was made available to us and was able to neutralize more than 5 logs of all 3 strains of virus.

TABLE IV. TITRATION OF ADAPTED AR 86 VIRUS IN 21-DAY MICE

Material	Virus dilution	Summary Died	Summary Lived	Titre, logs	A.S.T. (days)
21-day series, baby-mouse brain, 44th passage	1	6	0		6·2
	2	6	0		5·8
	3	6	0		5·5
	4	5	1	6·35	8·2
	5	4	2		9·3
	6	6	0		7·7
	7	1	4		13·0
21-day series, from 21-day-mouse brain, 44th passage	1	5	1		7·0
	2	6	0		6·7
	3	4	2		10·7
	4	3	3	3·82	10·5
	5	1	5		13·0
	6	0	6		14·0
	7	0	6		14·0
21-newborn staggered series, from baby mice, 55th passage	1	6	0		4·0
	2	6	0		3·8
	3	6	0		3·7
	4	6	0	6·0	4·8
	5	5	1		6·3
	6	3	3		11·3
	7	1	5		13·0

greater significance, however, is the difference in the average survival-time shown by the mice in these groups. This is shown in Table IV.*

From the results shown it is clear that both passage series have been sufficiently modified to ensure a high state of pathogenicity for young adult mice. From protection tests it was also clear that the adapted virus was unaltered in its immunologic reactions. Stocks of virus were prepared from the 60th passage in infant mice and have proved satisfactory for routine neutralization tests in 16-gm. adult white mice.

RELATION OF STRAINS AR 86 AND AR 169 TO SINDBIS VIRUS

When strain AR 86 was first isolated it was found that it behaved in a manner similar to that described by Dr. R. M. Taylor[1,5] for Sindbis virus. Application was made to him for some antiserum against this agent. This was provided and tests with it against the local isolates showed a degree of neutralization sufficient to establish that the viruses were closely related, and probably identical. Later, Dr. Taylor generously provided us with some lyophilized 7th-passage Sindbis virus, AR 339 strain. Cross-neutralization tests were done with this and the 3 South African isolates and they were found to be reciprocally and very nearly quantitatively cross-reactive. They are, therefore, closely related and probably identical.

The data obtained in some of the cross-neutralization tests which bring out this relationship are shown in Table V. Inspection of the figures shows that serum of the monkey immunized against AR 169 is consistently less able to neutralize all three strains than sera of the other two monkeys; this may be because the AR 169 monkey was immunized by subcutaneous inoculation while the other two received intracerebral doses of virus.

* Before inoculation all the 21-day mice were removed from their mothers and were randomized in two large boxes. This was done in the hope that resistant litters might be split up and also in order that there should be a more even distribution of mice, by size, throughout the experiment.

TABLE V. RESULTS OF CROSS-NEUTRALIZATION EXPERIMENTS WITH SINDBIS VIRUS

Serum	Virus: AR 86 Titre (log)	AR 86 Logs neut.	AR 169 Titre (log)	AR 169 Logs neut.	Sindbis Titre (log)	Sindbis Logs neut.
Sindbis Monkey Pre-inoculation	7·3		6·7		7·5	
Sindbis Immune	1·7	5·6	1·6	5·1	1·6	5·9
AR 169 immune	2·6	4·7	2·3	4·4	3·0	4·5
AR 86 Immune	2·0	5·3	1·0	5·7	1·6	5·9

Coxsackie Strains. Other neutralization experiments were set up against a number of immune sera supplied to us by the Coxsackie department of the Poliomyelitis Research Foundation Laboratories. These included antisera to the following Coxsackie strains: A1, A2, A3, A4, A5, A6, A7, A8, A9, A10, B1, B2, B3, B4, G10, G12, G13, G14 and G15. The only one of these to show any neutralizing power was A10, and subsequent experiments established that the neutralization in this case was due to a naturally-acquired Sindbis infection in the monkey used to provide the Coxsackie A10 serum. Another monkey which was non-immune to AR 86 virus was immunized against Coxsackie A10 virus and developed potent antibodies against that agent. Nevertheless this Coxsackie A10 antiserum had no neutralizing power for the AR 86 and AR 169 South African isolates. It is therefore concluded that the latter are unrelated to any of the Coxsackie strains mentioned above.

IMMUNITY IN MAN

It is not known whether these agents produce illness in man. A survey of immunity with sera collected from human beings residing in the Eastern Cape Province, Transvaal, Natal, Zululand and the Orange Free State is at present being made. The results will be reported later. It suffices here to say that neutralizing substances do occur in human sera.

The results obtained with the sera of the static non-European population at Isis Estates will now be referred to. The fact that all the members of this group are not truly indigenous to the area renders the interpretation of the results difficult. Sera collected from 160 persons residing at Isis Estates were tested against virus AR 169. Of these, 15 were found to be protective for that agent. These, and 46 that were not protective, were tested against AR 86 strain. All the sera tested gave similar results for both strains of virus.

Table VI lists the donors of 6 of these sera whose personal histories relate their acquisition of the neutra-

TABLE VI. DATA SHOWING INDIGENOUS CHARACTER OF SOME PERSONS FOUND TO POSSESS ANTIBODY AGAINST THE VIRUSES

Donor No.	Age (years)	Sex	Birthplace	Years resident at Isis Estates
1	6	M	Isis Estates	6
2	¾	F	Knoppiesfontein* ..	¾
3	35	M	Knoppiesfontein* ..	15
4	32	M	Rietfontein*	5
5	39	F	Onbekant*	1
6	33	M	Rietfontein*	20

* Knoppiesfontein, Rietfontein and Onbekant are names of adjacent and contiguous farms which constitute part of the same area.

lizing substances to the district in which Isis Estates is situated. Serum No. 1 was from a child of 6 who had spent his whole life at Isis Estates. Serum No. 2 was from a 6-months-old baby born on the boundary between Isis Estates and the neighbouring farm, Knoppiesfontein, who had never been off the Estate, and whose mother's serum was non-protective. Serum No. 3 was taken from a 35-year-old woman who was born on Knoppiesfontein, had lived on Isis Estates for 15 years, and had never left the district in her life. Serum No. 4 was from a 32-year-old man who had only been on Isis Estates for 5 years, but who was born at Rietfontein a few miles away, and had spent his whole life in the area. Serum No. 5 was from a 39-year-old woman, born at Onbekant, a neighbouring farm. Her last period of residence on Isis Estates was only 1 year, but her entire life had been spent either at Onbekant or on Isis Estates. Serum No. 6 was from a 33-year-old male born at Rietfontein but resident at Isis Estates for a period of 20 years. It is possible that the 3 men could have acquired their neutralizing substances elsewhere, but the two children could not have acquired their neutralizing substances anywhere else. It is also unlikely that the woman acquired her neutralizing substances anywhere but on Isis Estates. From these facts it appears that the virus attacks man and has recently done so at Isis Estates.

In an attempt to isolate virus from human beings a 'clinic' has been established and functions on the Estate once a week. Two of the authors (M.P.W. and R.H.K.) serve alternately, and attend those who report ill. Temperatures of all are taken and blood samples are collected from any with fever or suspicious symptoms, in order to provide material for virus study. Although this service has been in operation for almost a year we have seen only a few cases of febrile illness and have not yet succeeded in isolating any pathogenic agents from them.

SUMMARY

Three strains of filter-passing virus were isolated from Culicine mosquitoes caught near Johannesburg. The agents were originally pathogenic for infant but not for adult mice. One strain was successfully adapted to adults by serial intra-cerebral passage. Inoculation of the viruses into grivet monkeys, rabbits and guinea-pigs did not cause illness, but usually evoked the formation of antibody. The viruses are almost completely inactivated by heating for 30 minutes at 56°C, but not at 53°C. The lesions evoked by them in mice consist of diffuse myositis and acute encephalitis. Neutralization tests indicated that the virus strains are identical with each other, that they have no relation to any of 19 strains of Coxackie virus, but are closely related to, and perhaps identical with, Sindbis virus. Protection tests with sera from human beings indicate that the viruses have recently been active in man in the Babsfontein area not far from Johannesburg. The effects of the virus in man are, however, not known.

We are greatly indebted to Dr. James Gear, Director of the Poliomyelitis Research Foundation Laboratories, for his cooperation in providing many of the facilities required for this work; to Messrs. David Davis and K. H. Schulz for organising the capture of arthropods, and to Drs. Botha de Meillon and J. J. Steyn for the classification of them. We are also indebted to Dr. R. M. Taylor of N.A.M.R.U. III Laboratories, Cairo, Egypt, for the AR 339 strain of Sindbis virus, and to Dr. V. Measroch and Miss F. R. Prinsloo for the Coxsackie antisera and Coxsackie virus strain A 10. We should like to record our appreciation of the cooperation of Messrs. I. and A. L. Bader and Dr. Ian McFarlane, the resident veterinary officer, in our programme involving Isis Estates.

REFERENCES

1. Taylor, R. M., Rizk, F. and Kader, A. (1953): J. Egypt. Med. Assoc., **36**, 479.
2. Reed, L. J. and Muench, H. (1938): Amer. J. Hyg., **27**, 493.
3. Melnick, J. L. and Godman, G. C. (1951): J. Exp. Med., **93**, 247.
4. Godman, G. C., Bunting, H. and Melnick, J. L. (1952): Amer. J. Path., **28**, 223.
5. Taylor, R. M., Hurlbut, H. S., Work, T. H., Kingston, J. R. and Frothingham, T. E. (1955): Amer. J. Trop. Med. Hyg., **4**, 844.

VASCULAR PATTERNS IN TUMOURS OF THE EXTREMITIES*

M. B. M. DENNY, M.B., CH.B. (CAPE TOWN), D.M.R. (LOND.)

From the Departments of Radiology, King Edward VIII Hospital, Durban, Baragwanath Hospital, Johannesburg, and General Hospital, Johannesburg

The arteriographic investigations into the vascular patterns of tumours of the extremities which form the basis of this report have in the main been undertaken by the Radiological Unit of King Edward VIII Hospital, Durban, and more recently at the Baragwanath and General Hospitals, Johannesburg.

This paper is essentially a preliminary report, as it has become apparent during this work that a considerable number of cases will have to be investigated before reasonably final conclusions can be drawn. A few patterns have, however, appeared with sufficient constancy to be of value in differentiating malignant growths from benign neoplasms and from those of an inflammatory nature.

There are many types of tumours of the extremities, but attention has only been directed to those in which the investigation would appear to have a potential value in excluding malignancy.

History

Arteriography for the purpose of establishing vascular

* A paper presented at the South African Medical Congress, Pretoria, October 1955.

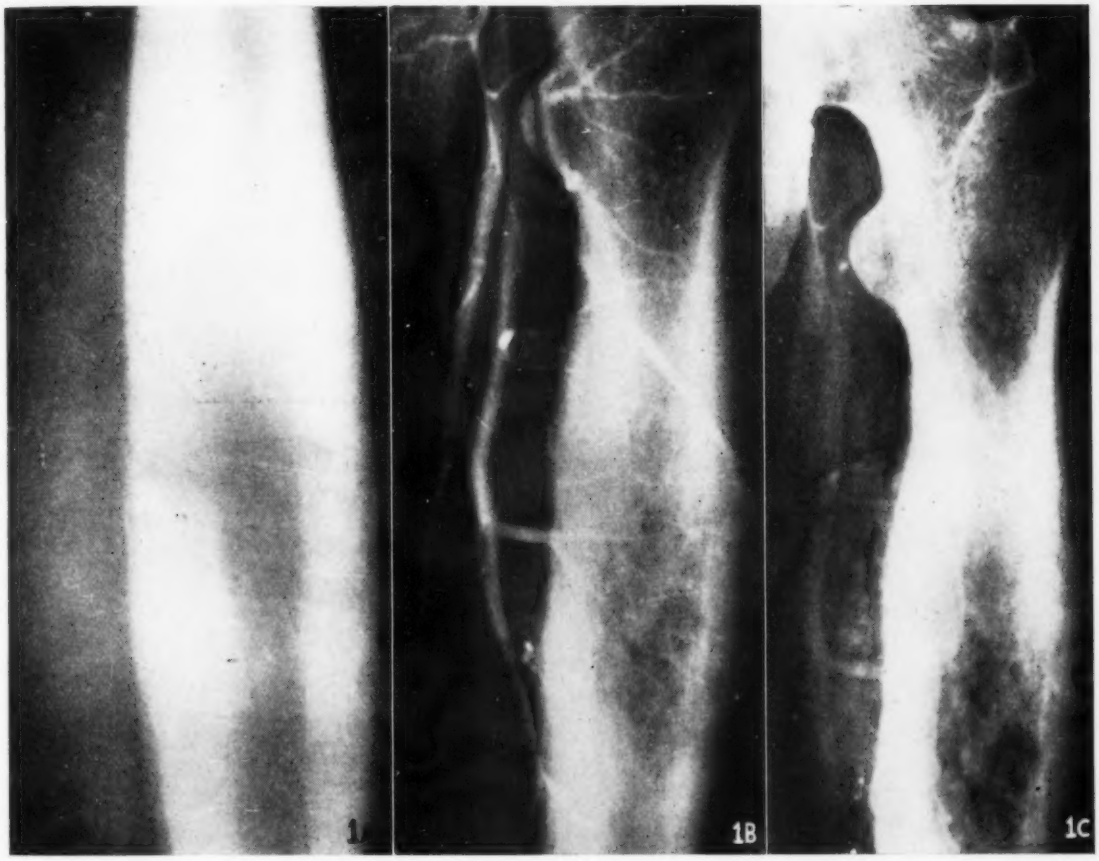


Fig. 1. Ewing's type of tumour of femur. Indian male aged 28, with 2 months' history of swelling of femur. Tumour was increasing in size and painful on palpation.

Fig. 1*A*. Plain film A.P. view, showing (i) fusiform widening of mid-shaft of femur, (ii) slight lamellar periostitis.

Fig. 1*B*. Arteriogram (first arterial phase, 3 seconds), showing (i) increased regional supply, (ii) small arteries ramifying in area of involved bone, (iii)mass of small vessels in tumour substance between trunk of profunda artery and medial cortex of femur.

Fig. 1*C*. Arteriogram (6 seconds), showing (i) residual arterial filling, (ii) increased prominence of vessels surrounding and within tumour area, (iii) early venous drainage, (iv) no localized venous blush as in subacute inflammatory lesions.

patterns of various tumours was first undertaken by Dos Santos, Lamas and Caldas[1] (1932), Reboul and Racine[2] (1934), and Farinas[3] (1937). Columella and Mucchi[4] (1937) also investigated the technique. The investigation was discontinued for lack of adequate contrast media but more recently interest has been revived by Columella and Mucchi[10] and papers by Inclan,[7] Dos Santos[5,6] and Sutton[8] have also appeared.

Varying conclusions have been presented and it is apparent that the investigation is still in its infancy.

Arteriographic investigation of tumours is a natural development of radiological investigation in the field of contrast media. It may ultimately present an alternative method to biopsy in the diagnosis of tumours, and possibly a safer method.

Material Investigated

Forty tumours were investigated, as follows:

Malignant Tumours: Fibrosarcoma (4), secondary sarcoma in neurofibroma (3), Kaposi haemorrhagic sarcoma (2), osteogenic sarcoma (sclerosing) (2), osteogenic sarcoma (osteolytic), secondary chondro sarcoma, Ewing-type tumour, malignant synovioma (1).

Benign Tumours: Aneurysms (6), osteoclastoma (3), angioma, neurofibroma, lipoma, bursal cyst, ossifying haematoma, congenital phlebectasia (1).

Inflammatory Lesions: Subacute inflammatory (7), chronic inflammatory (1).

Tumours with unknown histology but with conclusive clinical course (2).

Selection of Cases

Briefly, the cases were selected for the investigation of the following factors, although it is admitted that all of these indications have not as yet been fully explored:

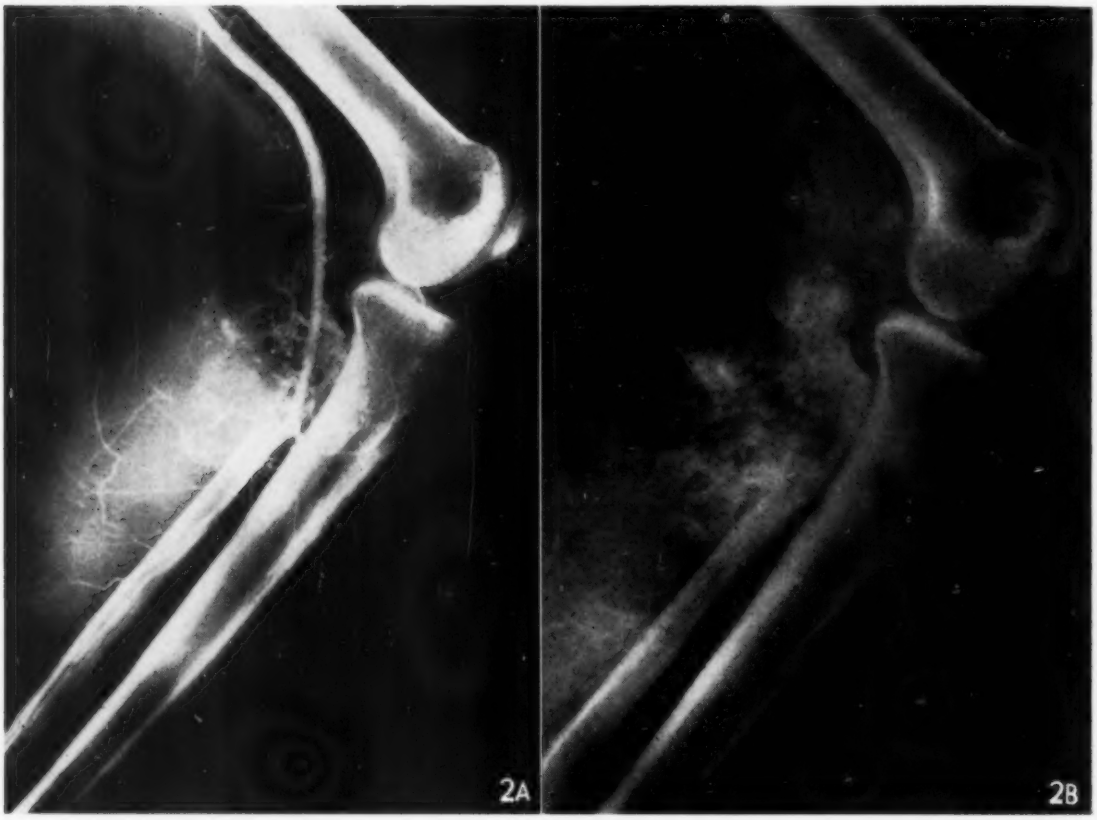


Fig. 2. Osteolytic osteogenic sarcoma.

Fig. 2*A*. Arteriogram (arterial phase, 2 seconds), showing (i) generalized increase of arterial ramification, (ii) stretching of vessels, (iii) early areas of pooling of dye.

Fig. 2*B*. Arteriogram (5 seconds), showing (i) grossly disordered vascular pattern, (ii) marked pooling of dye, (iii) marked venous drainage, (iv) extension of growth into lower calf, (v) diffuse staining of tumour.

1. To differentiate inflammatory from malignant lesions, and benign from malignant neoplasms.

2. To determine the onset of secondary malignant characteristics in tumours hitherto apparently benign.

3. As an aid to surgeons in the definition of vascular anomalies susceptible to surgical correction.

4. As a diagnostic aid in planning a radiotherapeutic approach in certain malignant lesions. This probably embraces the following points:

(*a*) Delimitation of tumour extension.

(*b*) Assessment of tumour anaplasia.

(*c*) Assessment of response to X-radiation in terms of vascular obliteration.

Technique

The introduction of percutaneous arteriography, both by the direct method and the Seldinger[9] catheter replacement method, has greatly increased the scope of vascular visualization. This has resolved into a relatively minor procedure easily accomplished by members of a radiological unit.

There is insufficient time to describe the details of our technique and I shall therefore content myself with enumerating what are considered to be the more important points:

1. Adequate periarterial infiltration with 2% procaine.

2. Transfixion of both walls of the artery, with subsequent slow withdrawal of the needle angling the point in the direction in which the dye is to be injected.

3. The use of 3-6 c.c. of 1% intra-arterial procaine immediately before the injection of the dye. This is particularly important in the brachial artery, which is extremely prone to spasm.

4. An absolute minimum amount of blood to be allowed into the needle or connecting system.

5. Strict attention to be paid to the establishment of a good puncture. Removal of the needle if doubt exists and repuncture after adequate compression.

6. Equally strict attention to be paid to the testing of

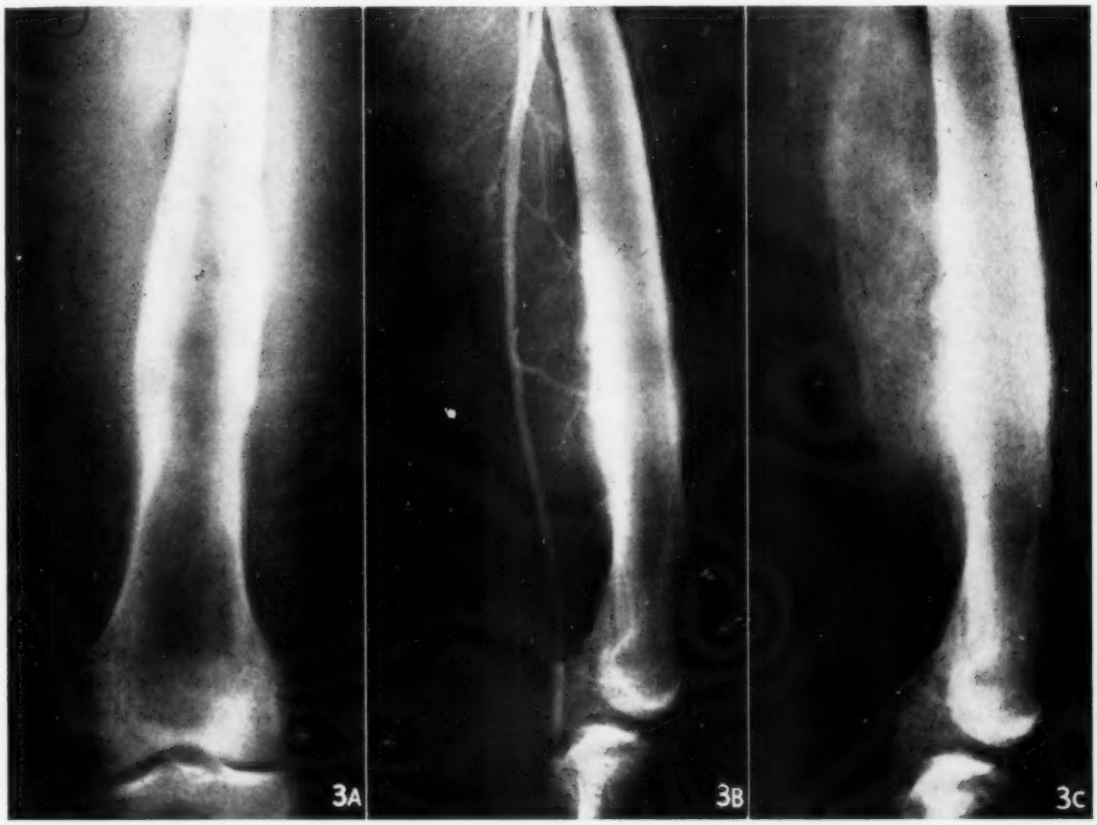


Fig. 3. Subacute inflammatory lesion of femur. Bantu male aged 42, with large fusiform mid-thigh swelling with small area of fluctuation in an otherwise firm tumour. Not warm. Leucocytosis of 10,000. Treated previously with penicillin with no response. Admitted as Ewing's-type tumour (4 months history).

Fig. 3*A*. Plain film, suggesting (i) lamellar new-bone formation surrounding the shaft and area of medullary destruction, (ii) sclerosis of bone in the tumour area, (iii) fusiform soft-tissueswelling.

Fig. 3*B*. Arteriogram (arterial phase), demonstrating no increase of regional supply and no abnormal vessels.

Fig. 3*C*. Arteriogram (6 seconds), showing localized crowded group of vessels surrounding tumour area. The appearance is probably due to venous congestion and is characteristicof a subacture inflammatory lesion.

the patient for dye sensitivity, and the completion of a consent form for examination by the patient.

Complications. Time also precludes a detailed consideration of complications, which in general are few and far between. *Contra-indications* are also few in number.

Radiation Protection. This is of importance in view of the increasing number of investigations of this type and should be strictly adhered to.

Apparatus. A rapid serial changer with accurate timing is of great value, but adequate films can usually be obtained on the conventional Bucky table.

INTERPRETATION OF ANGIOGRAMS

In the discussion of vascular changes in tumours of the extremities one is faced with the diametrically opposed statements of two workers. Columella and Mucchi[10] in their final summary state, 'The appearances in malignant tumours are so clear cut and characteristic that confirmation by biopsy can be dispensed with'. On the other hand Wagner[11] feels that he is unable to differentiate benign from malignant lesions or inflammatory lesions. Let me immediately say that neither statement appears to be tenable in the light of present-day knowledge as recorded in published literature.

Columella and Mucchi[10] have in all investigated 68 cases by arteriography, but supply no tabulated list indicating the number of cases of each condition. It is apparent that many of the investigations were carried out on syphilitic and tuberculous lesions and on the dystrophic osteopathies. From our own rather limited experience it is sufficiently clear that many of these

authors' statements are incomplete and their conclusions to a certain extent misleading.

Wagner[11] presents no satisfactory evidence to support his statement and his single case report is open to considerable criticism.

Our own views tend, at the present stage of this investigation, to be more conservative, agreeing with the views of Sutton[8] in a recently published and thoughtful article.

An initial observation on quantitative tumour vascularity may appropriately precede the more detailed review of abnormal vasculature: It is incorrect to consider all vascular tumours malignant and all benign tumours avascular in nature. Examples of benign vascular tumours are (*a*) osteoclastoma, (*b*) angioma, (*c*) neurofibroma (occasionally). Many of the slower growing, less anaplastic, spindle-cell sarcomata show minimal vascularity, but that which is present usually shows features of abnormality.

Pathological circulation of the malignant type we have found less easy to define than Columella and Mucchi[10] claim. These authors consider that malignancy is indicated by the following appearances:

'1. Increased regional circulation.

2. A rich vascular plexus presents no less in the depth than on the surface of the bone, with vessels both abnormal in size and distribution.

3. The presence of large vascular spaces in the tumour, which appear as irregular streaks of opaque material.

4. The presence of non-traumatic arterio-venous fistulae causing a great speeding up of circulation in the tumour, which is evidenced by simultaneous appearance in the connected arteries and veins of radio-opaque material in the first exposure.

5. Diffuse staining of the tumour.

6. The isosceles triangle of vascularity described by Farinas[3]—the so-called vascular paint-brush.'

From our experience it is clear that very few of the above findings need be present in a malignant tumour, and also that diffuse staining of the tumour does not necessarily indicate malignancy.

Arterio-venous fistulae need not necessarily show up in the first film, and can be presumed to be present even in the second and third film, provided both communicating venous and arterial elements are demonstrated clearly on the film.

Early venous filling is sometimes noted in the benign tumours of the vascular type, but subsequent to the completion of the arterial phase.

The expression 'abnormal vessel' is often used but no clear definition of this particular change in vasculature appears to have been supplied by previous writers. In our experience it has on occasions proved extremely difficult to come to a decision on this important point. The following features are in our opinion of significance apart from those already described:

1. A leash of vessel running through the tumour, often at right angles to normal vascular configuration.

2. Vessels as they branch normally show a progressively diminishing calibre; in malignant lesions, distal vessels may be larger than their parent vessels.

3. Vessels of peculiar configuration, as though imperfectly formed and possibly distorted by pressure of adjacent tumour, are suspect. These may well represent irregular channels lined by endothelialized tumour cells.

4. Abnormal stretching of a vessel seems to be seen more often within malignant tumours.

5. Abrupt terminations of moderately thick vessels, probably due to areas of infarction and thrombosis within the tumour.

6. Areas of mixed avascularity and vascularity within the tumour, especially when the avascular area is fluctuant, are highly suggestive of marked anaplasia and tumour necrosis.

7. A characteristic appearance (described by Inclan[7]) of radiating vessels running at right-angles to the cortical shaft, resembling spiculation of an osteogenic sarcoma. Inclan in fact considers this to be the early form of spiculation.

8. Abnormal tortuous draining veins in the later films are also suggestive of malignancy.

9. A vascular ring surrounding a relatively avascular area of tumour, as seen in some cerebral tumours, is a finding associated with malignant lesions.

There is a certain type of inflammatory lesion of a sub-acute variety, which is of particular importance in that, clinically, radiologically and often at operation, it frequently simulates the Ewing-type tumour. It is this lesion, presenting as it does as an ill-defined tumour, often in the mid-thigh, which of all inflammatory lesions presents the most difficulty in diagnosis. There is usually very little constitutional disturbance and little or no leucocytosis. Slight warmth if any is noted on palpation, and the tumour, although frequently firm, occasionally has areas of fluctuation, all of which may appear with the Ewing-type tumour.

Allen[12] has suggested, that this type of lesion, showing radiologically sclerosis, some destruction and often a lamellar periostitis, probably represents a recrudescence of a childhood osteomyelitis. We also believe that this appearance arises occasionally in cases inadequately treated with penicillin.

Previous writers have mentioned hyperaemia and slowing of circulation in cases of subacute osteitis. There is, however, a more clearly defined appearance associated with these lesions, consisting of a localized blush of crowded vessels of large calibre, usually with an inner concave margin. This is seen on films taken at about the 6-10 seconds period. In the first true arterial film a fine network corresponding to the subsequent pattern is often visible. The exact constitution of the later shadow is difficult to determine, but it probably consists of bloated and crowded veins with gross slowing of blood flow. This pattern has appeared constantly in those lesions which have ultimately proved to be inflammatory. In chronic osteomyelitis an arterial ischaemia and slight venous stasis are seen; in this respect other workers have made a similar finding.

A series of slides was then demonstrated, from which Figs. 1, 2 *and* 3 *have been selected for reproduction.*

I am indebted to Dr. S. Disler, Dr. J. Allen and Dr. K. Mills, Superintendents of the King Edward VIII Hospital, Baragwanath Hospital, and Johannesburg General Hospital respectively, for permission to present this paper.

I am especially grateful to Dr. M. Findlay, Chief Radiologist,

King Edward VIII Hospital, for her encouragement, and constructive criticism, and also to Dr. H. Clain and Dr. J. Kaye, Chief Radiologists of the Baragwanath and General Hospitals respectively, for permission to undertake these investigations in their departments.

I should also like to record my thanks to the numerous clinicians for their interest and cooperation, and to Miss M. McClaggen and Miss M. Tompkins of the departments of medical photography of the Wentworth Hospital, Durban, and the Johannesburg General Hospital respectively for the slide and photographic reproductions.

REFERENCES

1. Dos Santos, R., Lamas, C. and Caldas, P. (1932): Bull. Soc. nat. Chir., **48,** 635.
2. Reboul, H. and Racine, M. (1934): J. méd. franç., **23,** 122.
3. Farines, P. L. (1937): Radiology, **29**, 29.
4. Mucchi, L. and Columella, F. J. (1937): Quoted in reference 10.
5. Dos Santos, R. (1949): Lyon chir., **6,** 641.
6. *Idem* (1950): J. Bone Jt. Surg., **32B,** 17.
7. Inclan, A. (1942): *Ibid.*, **24,** 259.
8. Sutton, D. (1955): Brit. J. Radiol., **28,** 13.
9. Seldinger, S. I. (1953): Acta radiol., **39,** 368.
10. Mucchi, L. and Columella, F. J. (1951): J. Fac. Radiol., **3,** 135.
11. Wagner, F. B. (1951): Angiology, **2,** 6.
12. Allen, A. (1954): Personal communication.

TUBERCULOSIS IN NATAL

L. W. OSBURN M.B., B.CH.

Union Health Department, Tuberculosis Section

During the period June to November 1954, an X-ray tour of Western Natal was undertaken at the request of various local authorities. The itinerary included the towns of Estcourt, Colenso, Ladysmith, Newcastle, Dannhauser, Dundee, Glencoe, Greytown, Nottingham Road, Karkloof and Gillitts.

Unselected volunteers of all ages and racial groups and of both sexes were X-rayed at their own request. Many of the town employees live outside the municipal boundary but fall within a magisterial area, classed as a rural district. Urban and rural non-Europeans so intermingle that comparisons between population groups X-rayed would not be reliable.

A special group encountered included those who laboured in quarries, brickworks and other dusty occupations. It was intended to keep this data separate, for comparison with other groups, but it was found that Natives commonly work alternately on the mines and in other industries in this area, where there are many collieries dotted about. No higher rate of tuber-

TABLE I. DISTRIBUTION OF CASES BY RACE, SEX AND AGE

Age-Group (years)	*Europeans*			*Coloured*			*Indian*			*Native*		
	M	*F*	*Total*	*M*	*F*	*Total*	*M*	*F*	*Total*	*M*	*F*	*Total*
0–9												
X-rayed	884	849	1,733	78	90	168	629	581	1,210	928	1,059	2,023
Tuberculosis cases	0	1	1	0	0	0	0	1	1	8	2	10
%	0	0·1	0·06	0	0	0	0	0·2	0·09	0·9	0·2	0·4
10–19												
X-rayed	1,367	1,360	2,727	88	84	172	1,282	829	2,111	3,040	2,958	5,998
Tuberculosis cases	1	1	2	1	0	1	2	1	3	11	9	20
%	0·07	0·07	0·07	1·1	0	0·6	0·2	0·1	0·1	0·3	0·3	0·3
20–29												
X-rayed	388	214	602	16	27	43	263	122	385	2,401	597	2.998
Tuberculosis cases	1	1	2	1	0	1	2	0	2	31	2	33
%	0·3	0·5	0·3	6·2	0	2·3	0·7	0	0·5	1·3	0·3	1·1
30–39												
X-rayed	409	176	585	19	15	34	136	77	213	1,680	289	1,969
Tuberculosis cases	1	0	5	0	0	2	3	0	0	29	4	34
%	0·2	0	0·9	0	0	5·9	2·2	0	0	1·7	1·4	1·7
40–49												
X-rayed	203	144	347	12	4	16	74	47	121	1,027	184	1,211
Tuberculosis cases	1	0	1	0	0	0	3	0	3	29	4	33
%	0·5	0	0·3	0	0	0	4·1	0	2·4	2·8	2·2	2·7
50–59												
X-rayed	145	56	201	5	1	6	32	22	54	454	137	591
Tuberculosis cases	1	0	1	0	0	0	1	0	1	21	3	24
%	0·7	0	0·5	0	0	0	3·1	0	1·8	4·6	2·2	4·1
60 and over												
X-rayed	40	41	81	3	2	5	21	7	28	235	158	393
Tuberculosis cases	1	0	1	0	0	0	1	0	1	10	7	17
%	2·5	0	1·2	0	0	0	4·7	0	3·5	4·3	4·4	4·3
Total												
X-rayed	3,436	2,840	6,276	221	223	444	2,437	1,685	4,122	9,765	5,418	15,183
Tuberculosis cases	9	4	13	2	2	4	9	2	11	141	30	171
%	0·3	0·1	0·2	0·9	0·9	0·9	0·4	0·1	0·2	1·4	0·5	1·1

culosis was in fact detected in the group working in dusty occupation; a few cases in this group diagnosed as suffering from silicosis gave a mining history.

Many colliery managements requested the services of the mass X-ray unit. Findings in this group form the subject of a separate report.

Criteria for Diagnosis:

Initial diagnosis was made on the radiological appearance of the 70 mm. miniature film. Where no certain opinion could be given, the patient was recalled for large X-ray plates. In a minority of cases sputum tests were done.

Patients were diagnosed as having active tuberculosis if their X-ray plates presented certain characteristic features, viz:

1. Pleural effusion.
2. Primary or minimal tuberculosis.
3. Unilateral or bilateral pulmonary densities having the usual appearance and distribution of tuberculosis.
4. Pulmonary densities with cavitation.

Classification of positive cases by race, sex and age is given in Table I.

Within recent years the Union Health Department has organized a number of mass X-ray surveys and by various tours has provided urban and rural local authorities with X-ray facilities, often where they were lacking.

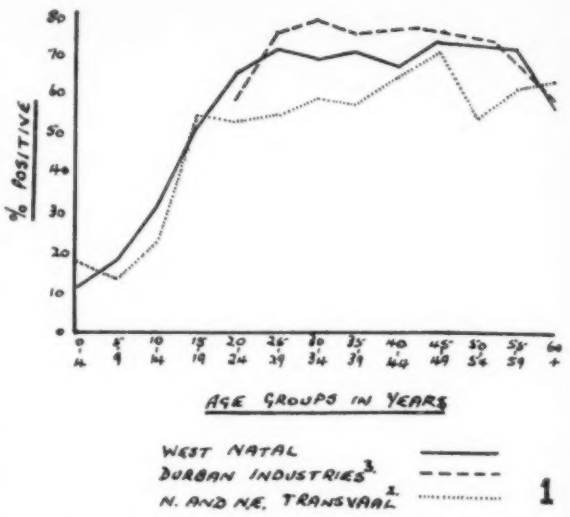


Fig. 1. Comparison of Mantoux results in Natives from (1) West Natal; (2) Durban (industries), (3) N. and N.E. Transvaal.

TABLE II. COMPARISON OF POSITIVE TUBERCULOSIS FINDINGS

Area and Author	*Age-Group*	*Europeans* No. X-Rayed	*Europeans* % Tub^{s}.	*Coloured* No. X-Rayed	*Coloured* % Tub^{s}.	*Indian* No. X-Rayed	*Indian* % Tub^{s}.	*Natives* No. X-Rayed	*Natives* % Tub^{s}.
Bechuanaland—Schechter[1]	All Ages	—	—	—	—	—	—	21,270	1·3
Western and North Western Cape—Osburn[5]	20 yrs and over	4,429	0·8	15,497	3·9	—	—	5,603	1·4
N. & E. Transvaal—Schneider[2]	15 yrs and over	—	—	—	—	—	—	3,918	1·5
Transkei—Wiles & Rabie[4]	16 yrs and over	—	—	—	—	—	—	16,105	2·9
West Natal—Osburn	20 yrs and over	1,816	0·5	104	2·9	801	0·9	7,162	2·0

Although much of the work was not done on statistically selected samples of the population, and was not planned as a survey, some idea of the prevalence of tuberculosis has been gained.

From recent reports, comparisons of the prevalence of tuberculosis in racial groups from different areas have been made in Table II.

TUBERCULIN TESTING

The procedure adopted was that described by Fine.[3] Test dose was 0·1 c.c. of 1/1000 P.P.D. solution injected intradermally into the forearm. A positive reaction was taken as an area of induration measuring not less than 6 mm. in diameter.

The results (for Natives) are shown by age in Table III. In Fig. 1 these results are compared in graphic form

TABLE III. REACTION TO MANTOUX TEST IN NATIVES BY AGE

Age-Group (years)	*Number tested*	*Number positive*	*% Positive*
0– 4	218	24	11·0
5– 9	1,465	267	18·2
10–14	1,431	477	33·2
15–19	326	161	49·3
20–24	199	131	65·8
25–29	187	133	71·1
30–34	134	92	68·6
35–39	257	181	70·3
40–44	63	42	66·7
45–49	49	37	75·5
50–54	22	9	40·9
55–59	31	22	70·9
60 and over	26	15	57·7
Total	4,408	1,591	36·3%

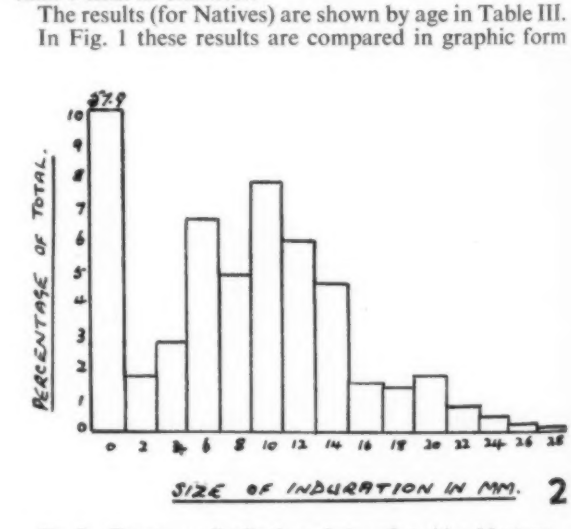


Fig. 2. Frequency distribution of size of positive Mantoux reactions.

with the findings obtained in Durban industries and in the Transvaal.

The frequency distribution of different sizes of the indurated area of the tuberculin reaction according to transverse diameter is shown for the present survey by the histogram in Fig. 2.

SUMMARY

A mass X-ray tour of Western Natal disclosed the following prevalence of active pulmonary tuberculosis in the population examined:

	Europeans	*Coloured*	*Indian*	*Native*
	%	%	%	%
All ages	0·2	0·9	0·2	1·1
Excluding children	0·5	2·9	0·9	2·0

Mantoux test were also carried out. Statistical tables and graphs are presented.

I thank the Secretary for Health for permission to publish this report and Dr. Dormer for his advice.

REFERENCES

1. Schechter, M. (1954): S. Afr. Med. J., **28**, 351.
2. Schneider, J. (1954): *Ibid.*, **28**, 689.
3. Fine, E.H. (1954): *Ibid.*, **28**, 34.
4. Wiles, F. J. and Rabie, C. J. (1955): *Ibid.*, **29**, 866.
5. Osburn, L. W. (1956): *Ibid.*, **30**, 613.

OFFICIAL ANNOUNCEMENT : AMPTELIKE AANKONDIGING

APPOINTMENT OF EDITOR

Applications are invited for the post of Editor of the *South African Medical Journal*. Applicants must be registered medical practitioners having knowledge and experience of medical journalism. A knowledge of languages will be a recommendation. The salary attaching to the post is on the scale £1,800×60—2,400, plus cost of living allowance of £352 for married men and £176 16s. 0d. for unmarried persons. (£100 of this allowance will be consolidated for pension purposes). The commencing notch will be according to experience, at the discretion of the Federal Council.

In addition to the Association's official *Journal*, the successful applicant will be required to edit the quarterly '*South African Journal of Laboratory and Clinical Medicine*'. He will also be required to join the Association's Superannuation Fund.

Applications, together with testimonials and a certificate of health, should be addressed to the undersigned to reach him before 31 August 1956.

A. H. Tonkin
Secretary

Medical House
35 Wale Street
Cape Town
19 May 1956

AANSTELLING VAN REDAKTEUR

Aansoeke word ingewag vir die betrekking van Redakteur van die *Suid-Afrikaanse Tydskrif vir Geneeskunde*. Applikante moet geregistreerde geneeshere wees met kennis en ondervinding van die geneeskundige joernalistiek. 'n Kennis van tale sal 'n aanbeveling wees. Die salaris aan die pos verbonde is op die skaal £1,800×60—2,400, plus 'n duurtetoeslag van £352 vir getroude mans en £176 16s. 0d. vir ongetroude persone. (£100 van hierdie toeslag sal vir pensioendoeleindes by die salaris gekonsolideer word.) Die beginsalaris sal na goeddunke van die Federale Raad met inagneming van vorige ondervinding vasgestel word.

Die applikant sal verwag word om benewens die redaksie van die Vereniging se amptelike *Tydskrif* ook dié van die kwartaalblad '*Suid-Afrikaanse Geneeskundige Tydskrif vir Laboratorium- en Kliniekwerk*' op hom te neem. Hy sal ook by die Vereniging se pensioenfonds moet aansluit.

Aansoeke, vergesel van getuigskrifte en 'n gesondheidsertifikaat, moet aan die ondergetekende gerig word om hom vóór 31 Augustus 1956 te bereik.

A. H. Tonkin
Sekretaris

Mediese Huis
Waalstraat 35
Kaapstad
19 Mei 1956

APPOINTMENT OF ASSISTANT SECRETARY

Applications are invited from bilingual, registered medical practitioners for the post of Assistant Secretary of the Medical Association of South Africa. Although the successful applicant may be required to work in the Transvaal, it is likely that he will be expected to spend some time initially at the Association's Head Office in Cape Town.

The salary attaching to the post is on the scale £1,250×50—1,750, plus cost of living allowance of £352 for married men and £176 16s. 0d. for unmarried persons. (£100 of this allowance will be consolidated for pension purposes). The commencing notch will be according to experience and will be determined by the Federal Council. The successful applicant will be required to join the Association's Superannuation Fund.

Applications, together with testimonials and a certificate of health, must reach the undersigned on or before 31 July 1956.

A. H. Tonkin
Secretary

Medical House
35 Wale Street
Cape Town
19 May 1956

AANSTELLING VAN ASSISTENT-SEKRETARIS

Aansoeke word ingewag van tweetalige geregistreerde geneeshere vir die betrekking van Assistent-Sekretaris van die Mediese Vereniging van Suid-Afrika. Alhoewel dit van die suksesvolle applikant vereis kan word om in die Transvaal te werk, sal hy waarskynlik verwag word om voorlopig 'n sekere tydperk by die Hoofkantoor van die Vereniging te Kaapstad deur te bring.

Die salaris aan die pos verbonde is op die skaal £1,250×50—1,750, plus 'n duurtetoeslag van £352 vir getroude mans en £176 16s. 0d. vir ongetroude persone. (£100 van hierdie toeslag sal vir pensioendoeleindes by die salaris gekonsolideer word.) Die aanvangskerf sal volgens ondervinding wees en sal deur die Federale Raad bepaal word. Van die suksesvolle applikant sal verlang word om by die Vereniging se pensioenfonds aan te sluit.

Aansoeke vergesel van getuigskrifte en 'n gesondheidsertifikaat moet die ondergetekende vóór of op 31 Julie 1956 bereik.

A. H. Tonkin
Sekretaris

Mediese Huis
Waalstraat 35
Kaapstad
19 Mei 1956

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

Albamycin. The Upjohn Company is making special emergency supplies of the new antibiotic, Albamycin, available to physicians without cost, for the treatment of critically ill patients. Albamycin is not yet available generally, but the manufacturers are making certain that no one who urgently needs the drug need be without it.

Albamycin is reported to be lethal to about 90% of common bacterial infections, and to be especially effective against staphylococci resistant to many of the antibiotics at present available. It is well tolerated by all age-groups and, when taken by mouth, it is rapidly absorbed, giving high blood concentrations.

Doctors desiring emergency supplies of Albamycin should apply to Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg, who are Upjohn's distributors in South Africa.

THE MEDICAL ASSOCIATION OF SOUTH AFRICA

BALANCE SHEET 31st DECEMBER, 1955

1954		£ s. d.	£ s. d.
	Accumulated Funds		
27,204	Balance, 31st December, 1954 ..	32,408 19 8	
5,205	Add: Surplus of Income over Expenditure for the Year	1,315 0 10	
32,409			33,724 0 6
	Funds—Capital Accounts		
257	National Health Services Emergency Fund		257 2 6
272	Balance, 31st December, 1954 ..	257 2 6	
15	*Less:* Delegates Expenses	— — —	
243	*Dr. H. A. Moffat Memorial Fund* ..		252 4 0
180	Balance, 31st December, 1954 ..	242 15 6	
63	Contributions Received during the Year	9 8 6	
	Liabilities		
4,106	Sundry Creditors		4,479 15 7
£37,015			£38,713 2 7

1954		£ s. d.	£ s. d.
	Fixed Assets		
7,279	Landed Property—'Byrness', Newlands Avenue, Newlands, Cape—At Cost		7,278 18 9
3,044	Office Furniture, Fixtures and Machines—Head Office and Johannesburg Agency		3,290 0 0
	Net Book Value		
3,195	1st January, 1953	3,195 0 0	
520	Purchased since that date (At Cost) less Sales (At Book Value)	1,131 11 8	
3,715		4,326 11 8	
671	Depreciation since 1st January, 1953..	1,036 11 8	
	Investments		
15,635	*Sundry Investments—At Cost* ..		15,635 0 0
(4,228)	Quoted Union Government Stock (Market Value, 31st December, 1955—£4,155)	4,335 0 0	
	Unquoted Shares	9,550 0 0	
	First Mortgage Bond	1,750 0 0	
	Current Assets		
9,151	Sundry Debtors, less Provision for Doubtful Debts (£600)		8,107 19 5
(350)			
1,406	Cash on Savings Account, Bank Current Account and on Hand ..		3,891 17 11
	Funds		
257	National Health Services Emergency Fund		257 2 6
	Cash at Bank		
243	Dr. H. A. Moffat Memorial Fund		
	Cash at Bank		252 4 0
£37,015			£38,713 2 7

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31st DECEMBER, 1955

1954		£ s. d.	£ s. d.
18,703	*Printing of Medical Journal*		20,426 17 11
943	*Printing of Laboratory and Clinical Medicine*		937 13 8
21,906	*Administration and Publication Expenses*		23,831 3 1
17,108	Salaries, Pension Fund, Unemployment Insurance and Pension ..	18,426 9 2	
977	Sundry Expenses	1,240 14 9	
1,035	Postages and Telegrams	1,107 7 8	
1,000	Rent	1,060 0 0	
623	Printing, Stationery and Office Requisites	797 17 1	
339	Depreciation of Office Furniture, Fixtures and Machines	365 4 0	
336	Wrappers	336 5 0	
288	Telephones	297 5 5	
200	Audit Fees	200 0 0	
4,093	*General Expenses*		4,681 17 6
	Travelling Expenses	3,783 2 4	
2,072	Delegates 2,715 17 0		
887	Staff 616 17 9		
—	Overseas Trip — Secretary.. .. 450 7 7		
378	Booklets and Questionnaires ..	530 19 2	
200	Entertainment Allowances	237 10 0	
15	Medals	109 5 6	
501	Expenses—'History of Medicine in South Africa'	16 10 6	
40	Bad Debts	4 10 0	
	Expenses—Public Relations Office, Johannesburg		2,217 15 5
500	*Grants to Universities for Library Services*		500 0 0
—	*Increase in Provision for Doubtful Debts*		250 0 0
5,205	*Surplus of Income over Expenditure transferred to Accumulated Funds Account*		1,315 0 10
£51,350			£54,160 8 5

1954		£ s. d.	£ s. d.
33,056	*Income from Medical Journal*		34,937 14 3
31,510	Advertising, less Commission ..	33,198 14 7	
1,452	Non-Members' Subscriptions	1,653 19 8	
94	Miscellaneous	85 0 0	
823	*Income from Laboratory and Clinical Medicine*		837 19 1
470	Subscriptions and Sales	572 9 6	
353	Advertising, less Commission ..	265 9 7	
10,479	*Members' Subscriptions*		10,954 7 3
2,898	*Agency Income*		3,348 18 10
4,094	*General Income*		4,081 9 0
3,501	Insurance Commission	3,067 2 7	
612	Interest on Investments	613 7 7	
385	Miscellaneous	280 9 7	
404	Rent less Expenses 'Byrness' ..	120 9 3	
(Net Expenditure)			
£51,350			£54,160 8 5

BENEVOLENT FUND

BALANCE SHEET 31st DECEMBER, 1955

1954 £		£ s. d.	£ s. d.
	Accumulated Funds		
40,664	Balance, 31st December, 1955 . . .	41,984 5 9	
£40,664		£41,984 5 9	

1954 £		£ s. d.	£ s. d.
	Assets		
	Investments at Cost		
7,068	*Union Government Stocks (Quoted)* (Market Value 31st December,		7,067 10 0
(6,767)	1955—£6,609)		
	£2,500 3½% 1962/65 . .	2,450 0 0	
	£1,500 3½% 1952/57 . .	1,492 10 0	
	£1,125 3% 1957/64 . .	1,125 0 0	
	£1,000 3% 1959/69 . .	1,000 0 0	
	£1,000 3% 1960/70 . .	1,000 0 0	
	Shares in Building Societies (Unquoted)		
28,550	Saambou (Permanente) Bouvereniging—14,700 Fully Paid-up Indefinite Shares of £1 each	14,700 0 0	28,550 0 0
	United Building Society—217 paid-up Permanent Shares of £50 each	10,850 0 0	
	South African Permanent Building Society—60 Paid-up Permanent Shares of £50 each	3,000 0 0	
3,500	*Secured Loan* . . . . . Medical House (Proprietary) Limited—First Mortgage on Medical House, Wale Street, Cape Town	3,500 0 0	3,500 0 0
596	*Sundry Debtors*		434 17 6
421	Interest Accrued	430 13 6	
	Medical Association of South Africa	4 4 0	
175	Medical House (Proprietary) Limited—Interest on Loan . .	– – –	
950	*Cash on Bank Current Account* . .		2,431 18 3
£40,664			£41,984 5 9

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31st DECEMBER, 1955

1954 £		£ s. d.	£ s. d.
2,315	*Benevolent Payments*	2,437 6 0	
22	*Stationery and General Expenses* . .	22 15 10	
£2,337			£2,460 1 10

1954 £		£ s. d.	£ s. d.
1,717	*Interest on Investments*		1,836 1 10
620	*Appropriation from Capital for Additional Benevolence*		624 0 0
£2,337			£2,460 1 10

ACCUMULATED FUNDS

1954 £		£ s. d.	£ s. d.
620	*Appropriation to Income and Expenditure Account for Additional Benevolence*	624 0 0	
40,664	*Balance, 31st December, 1955* . .	41,984 5 9	
£41,284			£42,608 5 9

1954 £		£ s. d.	£ s. d.
38,003	*Balance, 31st December, 1954* . .		40,663 17 8
3,281	*Contributions to Capital for the Year ended 31st December, 1955*		1,944 8 1
2,836	Donations	1,128 0 1	
246	Services Rendered	573 4 6	
199	Votive Cards	243 3 6	
£41,284			£42,608 5 9

REPORT OF THE AUDITORS TO THE MEMBERS OF THE MEDICAL ASSOCIATION OF SOUTH AFRICA

We have examined the books and accounts and vouchers of the Association and have satisfied ourselves of the existence of the securities. We have obtained all the information and explanations which, to the best of our knowledge and belief, were necessary for the purpose of our audit. In our opinion, proper books of account have been kept by the Association, so far as appears from our examination of those books.

The above Balance Sheet and attached Income and Expenditure Account are in agreement with the books of account. In our opinion, and to the best of our information and according to the explanations given to us, the said Accounts give the information required by the Companies Act 1926, as amended, in the manner so required and the Balance Sheet gives a true and fair view of the state of the Association's affairs as at 31st December, 1955, and the Income and Expenditure Account gives a true and fair view of the surplus for the year ended on that date.

Cape Town
12th June, 1956

Gurney, Notcutt & Fisher
Chartered Accounts (S.A.)
Auditors

BENEVOLENT FUND

We have examined the books and accounts and vouchers of the Benevolent Fund and satisfied ourselves of the existence of the Securities. The above Balance Sheet and attached Statements of Income and Expenditure and Accumulated Funds are in agreement with the books of account. In our opinion the Balance Sheet gives a true and fair view of the state of the Fund's affairs as at 31st December, 1955, and the Statements of Income and Expenditure and Accumulated Funds give a true and fair view of the Income and Expenditure of the Fund in respect of the year ended that date.

Cape Town
12th June, 1956

Gurney, Notcutt & Fisher
Chartered Accountants (S.A.)
Auditors

MEDICAL AID AND BENEFIT SOCIETIES

C. A. H. GREEN, M.B., B.CH. (OXON), M.R.C.S. (ENG.), L.R.C.P. (LOND.)

A considerable amount of time and money has recently been devoted by the Medical Association of South Africa to contract practice matters. It seems to me that a short memorandum on medical aid and benefit societies and their relation to the medical profession may serve a useful purpose.

The majority of contributors to medical aid societies are salaried persons, referred to as the white-collar brigade, typified by a clerk in an office. He joins a medical aid society in order to insure against the crippling cost of (1) prolonged illness, (2) illness requiring major surgical procedures, or (3) illness of an obscure nature requiring investigation.

Most medical aid societies are sponsored and subsidized by employers, who may themselves participate in the scheme. In the event of illness a member is frequently expected to bear anything up to 30% of the medical expenses, up to 40% of the hospital fees, and the total cost of medicines. Thus a serious illness may prove a considerable financial hardship to a member of a medical aid society, even though he is responsible only for a portion of the total costs.

The successful operation of medical aid societies enables a large number of doctors to earn considerable incomes from a group of people who, as individuals, would not be able to pay for these services. It is the stated policy of the Medical Association to encourage and foster the formation and development of medical aid societies for the middle-income group.

The majority of contributors to benefit societies or sick funds are daily-paid working men typified by a miner or factory employee. When this individual is ill his income ceases during the time he is off sick. He therefore contributes to a benefit society, which makes provision for sick-pay as well as for medical services. The majority of the members of benefit societies belong to the lower income groups of the people. In the case of serious illness they are not in a position to pay even a proportion of the doctor's accounts, or for medicines, or even a proportion of hospital costs. These benefits are therefore included as full benefits for members of a benefit society. In addition funeral expenses and a grant of a lump sum to the dependants of a member when he dies are paid, for obvious reasons. Benefit societies in this country actually function in practically the same manner as the National Health Service in Britain.

In order to function economically within the limits of their income from subscriptions, benefit societies have to contract with doctors, chemists and nursing homes for their services at reduced rates. Doctors are employed as medical officers on a part-time salary and are the king-pins of the financial structure of the benefit society. The medical officer signs the sick-pay forms, prescribes the medicine and authorizes hospital admissions. Irresponsible medical officers may and frequently have been the cause of a benefit society's costs becoming prohibitive. For this reason benefit societies are not keen on employing any or every doctor who happens to be on the Medical Register. The more doctors employed by a society relative to the numbers of the members the higher the administrative costs.

The successful functioning of benefit societies has meant that a large number of doctors have earned an assured, if not a considerable, income, earned admittedly the hard way, from a group of people who as individuals would prove very poor and erratic patients.

Without very heavy subsidies from the Government the lower income groups could not possibly operate a medical aid society scheme.

It has been my experience, which is not inconsiderable, that representatives of medical aid and benefit societies are only too willing to negotiate with the Medical Association and accede to any requests which in their opinion are reasonable. They wish to work in harmony with us, but it must not be forgotten that negotiation is a matter of give and take on both sides. Although these societies cannot do without us, we also as a profession cannot do without them.

MEDICAL DEGREES CONFERRED AT THE UNIVERSITY OF CAPE TOWN

The following Degrees were conferred at the Graduation Ceremony, University of Cape Town, on Friday, 29 June 1956:

Degree of Doctor of Medicine

Harry Tarley Phillips, M.B., Ch.B., D.P.H. (subject of thesis: 'An inter-racial study of trends in Public Health in the City of Cape Town'.)

Degree of Master of Medicine (Medicine)

Walter Beck, B.Sc. (Stell.), M.Sc., M.B., Ch.B.

Degree of Master of Obstetrics and Gynaecology

Pierre Francois Mulvihal du Toit, M.B., Ch.B.
Willem Hendrik Müller, M.B., Ch.B.

Degree of Master of Surgery

Arthur James Puttick, M.B., Ch.B.
Jacobus Petrus van Niekerk, M.B., Ch.B.

Degree of Bachelor of Medicine and Bachelor of Surgery

Ephraim Sheftel Benjamin.
Brian David Brokensha.
John Duncan Coxon.
George Fred Enslin, B.Sc.
Richard Tamplin Hart.
Roger Clifford Hindle.
Meyer Behr Hodes.
Ivor Newton Johnson.
Walter Joachim Kruger.
Ian Nevis MacLeod.
Jacobus Cornelius O'Kennedy, B.Sc. (Stell.).
Chunderaj Rajkumar Somers, B.Sc. (S.A.).
Andrew Louw Steyn.
Daniel Johannes van der Merwe, B.Sc. (O.F.S.).
Jacobus Gerhardus van Niekerk.
Linde Vanrenen.
Leon Arnold Weintrob.

M.B. B.Ch. DEGREES, UNIVERSITY OF THE WITWATERSRAND

The following candidates have completed all the requirements of the Sixth Professional Examination for the degree of M.B., B.Ch.:

Bhamjee, E. M.
Freinkel, A. L.
Karim, G. M.
Ordman, L. J.
Schmitt, M. E.
Senokoanyane, S. R.
Klopper, J. M. L.
Legum, C. P.
Luntz, C. H.
Malatskey, A.
Masibi-Langa, A. P. M.
Momoniat, M. I.
Sishuba, C. D. T.
Song, E.
van der Westhuizen, N. J. G.
Wallace, C.
Wong, A. K. C.

OPENING OF THE KARL BREMER HOSPITAL

The £1,260,000 Karl Bremer Hospital at Bellville, designed to provide accommodation for 386 beds, including 26 for children, was formally opened by the Minister of Health, the Hon. J. F. T. Naudé on Saturday, 30 June 1956. About 2,500 people attended the ceremony. The Minister said the cost of each bed in the hospital had been £3,000.

Mr. Naudé said increasingly expensive medicines were coming into use in hospitals which, on paper, seemed to throw a greater burden on taxpayers. In fact, expensive drugs and remedies meant quicker healing and therefore more room for sick people in the hospitals.

They increased the efficiency and turnover of hospitals, but he wanted to warn medical men and chemists, both in the public service and in private practice, that people were becoming irritated at the high cost of medicine. It would be tragic if the cost of healing became too high for the ordinary man.

Mr. Naudé said the Karl Bremer Hospital was a modern institution of which South Africa could be proud.

A fuller version of the Minister's address will be published in the *Journal* next week.

PASSING EVENTS : IN DIE VERBYGAAN

Dr. F. v. d. M. Badenhorst, M.B., Ch.B. is met ingang 1 Julie 1956 aangestel as distriksgeneesheer van Stellenbosch.

* * *

Dr. J. Carstens,, M.B. Ch.B., D.A., formerly of Groote Schuur Hospital and the Lewisham Hospital, London, now Senior Lecturer in Anaesthetics at the Karl Bremer Hospital, Bellville, has started practice in Cape Town as a specialist anaesthetist at 25 Keurboom Road, Newlands. Telephones: Rooms 69–2924, Residence 9–79354.

* * *

Dr. J. Carstens, M.B., Ch.B., D.A., voorheen van Groote Schuur Hospitaal en die Lewisham-hospitaal, Londen, en tans Senior Lektor in die Narkose by die Karl Bremer Hospitaal te Bellville, praktiseer nou in Kaapstad as spesialis-narkotisent te Keurboomweg 25, Nuwelande, Kaapstad. Telefone: Spreekkamers 69–2924, Tuis 9–79354.

* * *

Dr. Peter A. Caswell, M.B., B.Ch. (Rand), D.A., R.C.P. & S. (Irel.), D.A., R.C.P. & S. (Eng.) is now practising as a specialist anaesthetist at 309 Harley Chambers, Jeppe Street, Johannesburg, in partnership with Drs. G. Hochschild, F. W. Roberts and M. S. Kramer. Telephones: rooms 22-8614, 22-6553, residence 41-2432, emergency 22-4191.

REVIEWS OF BOOKS : BOEKRESENSIES

EXERCISES BEFORE AND AFTER CHILDBIRTH

Before and After Childbirth. Ante-Natal and Post-Natal Exercises. By Jane Madders, M.C.S.P., Dip.Phys.Ed. Pp. 31, with illustrations. 3s. Edinburgh and London: E. & S. Livingstone Ltd. 1955.

Contents: 1. Ante-Natal. 2. Procedures and Postures for Normal Labour. 3. Post-Natal.

This booklet consists mainly of photographs to illustrate exercises which can be performed with benefit both before and after labour. The text is confined to short explanations of the 'why' and 'how' of the exercises.

The emphasis is on relaxation and the booklet could well be recommended to mothers and mothers-to-be, who will find it both interesting and useful.

A.H.T.

PORPHYRIN

Porphyrin Biosynthesis and Metabolism. By G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Elaine C. P. Millar, A.H.W.C., A.R.I.C. Pp. 308 with 70 illustrations. 30s. net. London: J. & A. Churchill Ltd. 1955.

Contents: The succinate-glycine cycle. Some properties of 8-aminolaevulic acid dehydrase. The metabolism of 8-aminolaevulic acid. Haem and porphyrin formation from glycine, 8-aminolaevulic acid and porphobilinogen. The rôle of some porphyrins and porphyrin precursors in the biosynthesis of haem. On the synthesis and metabolism of C^{14}-labelled hematoporphyrin. Independent biosynthesis of different haemin chromo-proteins, with special reference to cytochrome c: the rôle of tissue organs. Experimental studies of porphyrin metabolism in cyto-chrome c synthesis. Porphrin and chlorophyll biosynthesis in chlorella. Heterogeneous metabolism of haemoglobins. Cellular formation of intermediates during haemoglobin synthesis. Relation of free erythrocyte porphyrins to haemoglobin biosynthesis. Studies of some liver heme proteins and porphyrins in experimental sedormid porphyria. Studies of porphyrins in animals with experimental hepatic porphyria. Metabolism of porphobilinogen and of porphyrins in the rabbit. Precursors of porphyrin and porphobilinogen. Studies on the mechánism of porphyrin biosynthesis with the aid of inhibitors. The formation of porphyrins by photosynthetic bacteria. The synthesis of the uroporphyrins II and IV. General discussion.

This volume records in 20 papers and discussion the rapid developments which have taken place in our knowledge of the biosynthesis of porphyrins since the subject was discussed at a Ciba Foundation conference in 1951. A discussion of the porhyria diseases was deliberately excluded but there are several communications on the experimental production of porphyria in rabbits by the administration of sedormid and allied compounds. The clinical symptoms and biochemical findings in experimental porphyria are identical with the acute porphyria in humans. However, the light that these studies might throw on the normal biosynthetic process rather than the relation to the porphyria diseases receives prior consideration.

The biosynthesis of porphyrins has been clarified recently in studies by Shemin and his co-workers of the Department of Biochemistry, Columbia University. Together with work by Neuberger, Rimington and others on closely allied problems it represents one of the major achievements of recent biochemical research. The early stages in the biosynthesis of porphyrins, i.e. the synthesis of porphobilinogen from such comparatively simple substances as glycine and succinic acid has been worked out. The further stages to haem formation are still somewhat uncertain. As the Chairman remarked in the closing discussion: 'The porphyrins, uroporphyrin, coproporphyrin and even protoporphyrin are at present like slippery stepping-stones. We can get across to haem but not without getting our feet wet'. The moment at which iron enters into the picture and the mechanism of its incorporation are also still undecided.

Most of the language in this volume will be intelligible only to the biochemist but for those who can read it it makes as fascinating a story as anything in modern biochemistry.

H.Z.

A HANDBOOK OF OPERATIVE SURGERY

A Handbook of Operative Surgery. Surgery of the Stomach and Duodenum. Second Revised Edition. By Claude E. Welch, M.D., D.Sc. (Hon.). Pp. 370, with 79 plates. $9.00. Chicago: The Year Book Publishers, Inc. 1955.

Contents: 1. Anatomy of Stomach and Duodenum. 2. Historical Summary. 3. Pre- and Postoperative Treatment; Anesthesia. 4. Special Instruments. 5. Incisions and Closure. 6. Congenital Abnormalities. 7. Perforating Wounds. 8. Gastrotomy and Duodenotomy. 9. Gastrostomy. 10. Diverticula of the

Stomach and Duodenum. 11. Hiatus Hernia. 12. Pyloroplasty and Cardioplasty. 13. Side-to-Side Anastomoses. 14. Duodenal and Gastric Ulcer. 15. Other Operations for Complications of Ulcer. 16. Gastric Cancer. 17. Tumours of the Duodenum. 18. Complications of Gastric Resection. 19. Late Complications of Gastric Operations. 20. Anastomosis with Special Clamps. 21. Duodenal Fistula. Appendices. Bibliography. Index.

As a series of clear illustrations to supplement a good text-book of surgery in its approach to the stomach and duodenum, this book is satisfactory. The new chapter on Hiatus Hernia is well done. Otherwise in the reviewer's opinion, it fails badly as a handbook of operative surgery. Surely even a 'young' surgeon does not welcome 15 pages of text and illustrations of 5 different ways of making a gastrostomy!

One page of arbitrary 'post-operative diets' is the only tribute to the effects of adequate post-operative care in the whole book. An incomplete page of some laboratory values is useless. The suggestion—with illustrations—of the use of squares of Gelfoam for tamponade of a duodenal ulcer overlying the gastroduodenal artery seems fantastic, or even dangerous.

This book should be used only by surgeons experienced in gastro-intestinal surgery. R.D.H.B.

CORRESPONDENCE : BRIEWERUBRIEK

KERATOPLASTY

To the Editor: The National Council for the Blind is taking an active interest in keratoplasty (corneal grafting) as a means of restoring a measure of sight to those who may benefit thereby. To this end it has undertaken two immense tasks.

The first is to arrange for a survey of all those persons already classified as blind or likely to become blind from corneal lesions so as to select as many as possible who may benefit by corneal surgery.

The other is to obtain as much corneal material as possible as easily as possible. The most plentiful source is from donors soon after death. The public have become aware of this and are coming forward readily in large numbers to donate their eyes. In this aspect medical men will be of great assistance in advising prospective donors and in expediting the delivery of grafting material as soon after death as possible.

An eye should be removed within four hours of death for storage in suitable surroundings and such a cornea can be used up to four days after death (i.e. in storage).

Now the number of people who will benefit from such operations is limited and they must be carefully selected. The amount of corneal material, on the other hand, which is theoretically available is far in excess of requirements. One should therefore, encourage people to donate their eyes on death because one can assure them there is only a slender chance of the eye actually being required and of being removed after death. This may cheer the next of kin.

But it is important when donating eyes to let it be known not only in the will but also to the next of kin and the family doctor or any doctor who may attend at an illness or operation, so that he (the doctor) may set in motion as early as possible the machinery for removing and storing the eye in the event of death. The donor should leave a notice of his intention with the local office of the National Council for the Blind by filling in a printed form giving the necessary details for the records. A register is kept of such donors. There will be a central depot in large centres where corneal grafting is undertaken which will arrange for the collection and storage of such eyes, as the need arises. The National Council for the Blind is keeping the register in various centres.

There are other means of obtaining corneal material provided for by the Act but this letter deals only with the case of the donor who dies in his own home or a private hospital. The law enacted for the purpose still retains many safeguards against abuse and impropriety, and the provisions are cumbersome. Nevertheless, with cooperation from those interested in corneal grafts and those in contact with donors, loss of time, which is the most serious obstacle, can be reduced to a minimum.

J. G. Louw
Hon. Secretary
Ophthalmological Society of South Africa

17 Church Square
Cape Town
20 June 1956

POLIO VACCINE

To the Editor: We have a rural practice which has been established for 4 years, about 40 miles from Port Elizabeth. Previously the great majority of our patients had their own private practitioners in Port Elizabeth. It has now been brought to our notice that some of these practitioners have recently written notes to certain of our private patients advising them about having their children immunized against poliomyelitis through the Municipal Health Scheme in Port Elizabeth.

We feel that this is unethical because: (1) All these practitioners are fully aware of the fact that these are our private patients and they are only occasionally consulted *re* a confinement or for some treatment for which we have no facilities here, usually without contacting us about it. We have ignored the latter because we do not want to tie our patients down. After gaining our information about the polio vaccine from the public press we have arranged for a supply of vaccine for those patients who approached us. For our needy patients we have arranged with the local health authorities to receive the necessary supply, free of charge.

(2) We feel that writing notes to patients is definitely canvassing.

(3) These patients do not fall within the Municipal area of Port Elizabeth and they, therefore, are not lawfully entitled to be immunized through the Municipal Health Scheme.

We would appreciate it if you could publish this letter as there might be other rural general practitioners in a similar position.

L. M. Oosthuizen
C. J. H. Steenkamp

P.O. Box 32
Sunland
18 June 1956

DIETARY FATS AND ARTERIO-SCLEROSIS

To the Editor: There has been much work carried out recently which incriminates fats, in particular the saturated animal fats, as a factor in the production of arteriosclerosis.

Much of the evidence is, perforce, statistical; inevitably so, as one can appreciate the difficulties associated with controlled dietetic experiment over 20, 30 or more years.

We have in our midst, however, comparatively large numbers of strict vegetarians, who have never included fats of this nature in their diet. The investigation of lipoid metabolism and the incidence of arterio-sclerosis in such individuals, as compared with the rest of the population of the same age group, would, I believe, give us far more direct evidence than say, comparison between the eating habits of the European and the Bantu, where many other factors may well play a part.

Philip Boekstein

P.O. Box 29
Livingstone
21 June 1956

CHARGES FOR DIVERSION OF TELEPHONE CALLS

To the Editor: I would refer to the announcement regarding the charges for the diversion of telephone calls which appeared in your issue of 9 June, and would advise that the Secretary of the South-West African Branch of the Association states:

'Charges for diversion of calls in South-West Africa published in *Official Gazette Extraordinary* of 16 March 1949, are as follows:

"10s. per mensem or portion thereof. If the period of diversion does not exceed 12 hours, 1s. per each such short period."

'Above charges are still in force in South-West Africa and are not affected by the change in the Union.'

A. H. Tonkin
Secretary
Medical Association of South Africa

Medical House
Cape Town
27 June 1956